12AP1/E5 -- Viventia Biotech
1964 -- Aventis
20K growth hormone -- AMUR
28P6/E6 -- Viventia Biotech
3-Hydroxyphthaloyl-beta-lactoglobulin –
4-IBB ligand gene therapy –
64-Cu MAb conjugate TETA-1A3 -- Mallinckrodt Institute of Radiology
64-Cu MAb conjugate TETA-cT84.66
64-Cu Trastuzumab TETA conjugate – Genentech
A 200 -- Amgen
A10255 – Eli Liliy
A1PDX – Hedral THerapeutics
A6 -- Angstrom
aaAT-III -- Genzyme
Abciximab -- Centocor
ABI.001 – Atlantic BioPharmaceuticals
ABT-828 – Abbott
Accutin
Actinohivin
activin -- Biotech Australia, Human Therapeutics
activin -- Curis
AD 439 – Tanox
AD 519 – Tanox
Adalimumab -- Cambridge Antibody Tech.
Adenocarcinoma vaccine – Biomira -- NIS
Adenosine A2B receptor antagonists -- Adenosine Therapeutics
ADP-001 – Axis Genetics
AF 13948 – Affymax
Afelimomab – Knoll
AFP-SCAN – Immunomedics
AG 2195 – Corixa
agalsidase alfa -- Transkaryotic Therapies
agalsidase beta -- Genzyme
AGENT– Antisoma
AI 300 – AutoImmune
AI-101 – Teva
AI-102 – Teva
AI-201 – AutoImmune
AI-301 – AutoImmune
AIDS vaccine – ANRS, CIBG, Hesed Biomed, Hollis-Eden, Rome, United Biomedical, American Home Products, Maxygen
airway receptor ligand -- IC Innovations
AJvW 2 -- Ajinomoto
AK 30 NGF -- Alkermes
Albuferon -- Human Genome Sciences
albumin – Biogen, DSM Anti-Infectives, Genzyme Transgenics, PPL Therapeutics, TranXenoGen, Welfide Corp.
aldesleukin -- Chiron
alefacept -- Biogen
Alemtuzumab –
Allergy therapy -- ALK-Abello/Maxygen, ALK-Abello/RP Scherer
allergy vaccines -- Allergy Therapeutics
Alnidofibatide -- Aventis Pasteur
Alnorine -- SRC VB VECTOR
ALP 242 -- Gruenenthal
Alpha antitrypsin -- Arriva/Hyland Immuno/ProMetic/Protease Sciences
Alpha-1 antitrypsin – Cutter, Bayer, PPL Therapeutics, Profile, ZymoGenetics, Arriva
Alpha-1 protease inhibitor -- Genzyme Transgenics, Welfide Corp.
Alpha-galactose fusion protein – Immunomedics
Alpha-galactosidase A -- Research Corporation Technologies
Alpha-glucosidase – Genzyme, Novazyme
Alpha-lactalbumin
Alpha-L-iduronidase -- Transkaryotic Therapies, BioMarin
alteplase -- Genentech
alvircept sudotox -- NIH
ALX1-11 –sNPS Pharmaceuticals
Alzheimer's disease gene therapy –

FIG. 1A

AM-133 -- AMRAD
Amb a 1 immunostim conj. -- Dynavax
AMD 3100 – AnorMED -- NIS
AMD 3465 – AnorMED -- NIS
AMD 3465 – AnorMED -- NIS
AMD Fab -- Genentech
Amediplase – Menarini, Novartis
AM-F9
Amoebiasis vaccine
Amphiregulin -- Octagene
anakinra -- Amgen
analgesic -- Nobex
ancestim -- Amgen
AnergiX.RA – Corixa, Organon
Angiocidin -- InKine
angiogenesis inhibitors -- ILEX
AngioMab – Antisoma
Angiopoietins -- Regeneron/Procter & Gamble
angiostatin -- EntreMed
Angiostatin/endostatin gene therapy – Genetix Pharmaceuticals
angiotensin-II, topical -- Maret
Anthrax -- EluSys Therapeutics/US Army Medical Research Institute
Anthrax vaccine
Anti platelet-derived growth factor D human monoclonal antibodies -- CuraGen
Anti-17-1A MAb 3622W94 -- GlaxoSmithKline
Anti-2C4 MAb -- Genentech
anti-4-1BB monoclonal antibodies -- Bristol-Myers Squibb
Anti-Adhesion Platform Tech. -- Cytovax
Anti-adipocyte MAb -- Cambridge Antibody Tech./ObeSys
antiallergics -- Maxygen
antiallergy vaccine -- Acambis
Anti-alpha-4-integrin MAb
Anti-angiogenesis monoclonal antibodies -- KS Biomedix/Schering AG
Anti-B4 MAb-DC1 conjugate -- ImmunoGen
Anti-B7 antibody PRIMATIZED -- IDEC
Anti-B7-1 MAb 16-10A1
Anti-B7-1 MAb 1G10
Anti-B7-2 MAb GL-1
Anti-B7-2-gelonin immunotoxin –
Antibacterials/antifungals -- Diversa/IntraBiotics
Anti-beta-amyloid monoclonal antibodies -- Cambridge Antibody Tech., Wyeth-Ayerst
Anti-BLyS antibodies -- Cambridge Antibody Tech. /Human Genome Sciences
Antibody-drug conjugates -- Seattle Genetics/Eos
Anti-C5 MAb BB5-1 -- Alexion
Anti-C5 MAb N19-8 -- Alexion
Anti-C8 MAb
anticancer cytokines -- BioPulse
anticancer matrix – Telios Integra
Anticancer monoclonal antibodies – ARIUS, Immunex
anticancer peptides – Maxygen, Micrologix
Anticancer prodrug Tech. -- Alexion Antibody Technologies
anticancer Troy-Bodies -- Affite -- Affitech
anticancer vaccine -- NIH
anticancers -- Epimmune
Anti-CCR5/CXCR4 sheep MAb -- KS Biomedix Holdings
Anti-CD11a MAb KBA –
Anti-CD11a MAb M17
Anti-CD11a MAb TA-3 –
Anti-CD11a MAb WT.1 –
Anti-CD11b MAb -- Pharmacia
Anti-CD11b MAb LM2
Anti-CD154 MAb -- Biogen
Anti-CD16-anti-CD30 MAb -- Biotest
Anti-CD18 MAb -- Pharmacia
Anti-CD19 MAb B43 –
Anti-CD19 MAb -liposomal sodium butyrate conjugate –

FIG. 1B

Anti-CD19 MAb-saporin conjugate –
Anti-CD19-dsFv-PE38-immunotoxin –
Anti-CD2 MAb 12-15 –
Anti-CD2 MAb B-E2 -- Diaclone
Anti-CD2 MAb OX34 –
Anti-CD2 MAb OX54 –
Anti-CD2 MAb OX55 –
Anti-CD2 MAb RM2-1
Anti-CD2 MAb RM2-2
Anti-CD2 MAb RM2-4
Anti-CD20 MAb BCA B20
Anti-CD20-anti-Fc alpha RI bispecific MAb – Medarex, Tenovus
Anti-CD22 MAb-saporin-6 complex –
Anti-CD3 immunotoxin –
Anti-CD3 MAb 145-2C11 -- Pharming
Anti-CD3 MAb CD4IgG conjugate -- Genentech
Anti-CD3 MAb humanised – Protein Design, RW Johnson
Anti-CD3 MAb WT32
Anti-CD3 MAb-ricin-chain-A conjugate –
Anti-CD3 MAb-xanthine-oxidase conjugate –
Anti-CD30 MAb BerH2 -- Medac
Anti-CD30 MAb-saporin conjugate
Anti-CD30-scFv-ETA'-immunotoxin
Anti-CD38 MAb AT13/5
Anti-CD38 MAb-saporin conjugate
Anti-CD3-anti-CD19 bispecific MAb
Anti-CD3-anti-EGFR MAb
Anti-CD3-anti-interleukin-2-receptor MAb
Anti-CD3-anti-MOv18 MAb -- Centocor
Anti-CD3-anti-SCLC bispecific MAb
Anti-CD4 idiotype vaccine
Anti-CD4 MAb – Centocor, IDEC Pharmaceuticals, Xenova Group
Anti-CD4 MAb 16H5
Anti-CD4 MAb 4162W94 -- GlaxoSmithKline
Anti-CD4 MAb B-F5 -- Diaclone
Anti-CD4 MAb GK1-5
Anti-CD4 MAb KT6
Anti-CD4 MAb OX38
Anti-CD4 MAb PAP conjugate -- Bristol-Myers Squibb
Anti-CD4 MAb RIB 5-2
Anti-CD4 MAb W3/25
Anti-CD4 MAb YTA 3.1.2
Anti-CD4 MAb YTS 177-9
Anti-CD40 ligand MAb 5c8 -- Biogen
Anti-CD40 MAb
Anti-CD40 MAb 5D12 – Tanox
Anti-CD44 MAb A3D8
Anti-CD44 MAb GKWA3
Anti-CD44 MAb IM7
Anti-CD44 MAb KM81
Anti-CD44 variant monoclonal antibodies -- Corixa/Hebrew University
Anti-CD45 MAb BC8-I-131
Anti-CD45RB MAb
Anti-CD48 MAb HuLy-m3
Anti-CD48 MAb WM-63
Anti-CD5 MAb -- Becton Dickinson
Anti-CD5 MAb OX19
Anti-CD6 MAb
Anti-CD7 MAb-PAP conjugate
Anti-CD7 MAb-ricin-chain-A conjugate
Anti-CD8 MAb – Amerimmune, Cytodyn, Becton Dickinson
Anti-CD8 MAb 2-43
Anti-CD8 MAb OX8
Anti-CD80 MAb P16C10 -- IDEC
Anti-CD80 MAb P7C10 -- ID Vaccine
Anti-CD8-idarubicin conjugate
Anti-CEA MAb CE-25
Anti-CEA MAb MN 14 – Immunomedics
Anti-CEA MAb MN14-PE40 conjugate – Immunomedics
Anti-CEA MAb T84.66-interleukin-2 conjugate
Anti-CEA sheep MAb -- KS Biomedix Holdings

FIG. 1C

Anti-cell surface monoclonal antibodies -- Cambridge Antibody Tech. /Pharmacia
Anti-c-erbB2-anti-CD3 bifunctional MAb -- Otsuka
Anti-CMV MAb -- Scotgen
Anti-CTLA-4 MAb
Anti-EGFR catalytic antibody -- Hesed Biomed
anti-EGFR immunotoxin -- IVAX
Anti-EGFR MAb -- Abgenix
Anti-EGFR MAb 528
Anti-EGFR MAb KSB 107 -- KS Biomedix
Anti-EGFR MAb-DM1 conjugate -- ImmunoGen
Anti-EGFR MAb-LA1 –
Anti-EGFR sheep MAb -- KS Biomedix
Anti-FAP MAb F19-I-131
Anti-Fas IgM MAb CH11
Anti-Fas MAb Jo2
Anti-Fas MAb RK-8
Anti-Flt-1 monoclonal antibodies -- ImClone
Anti-fungal peptides -- State University of New York
antifungal tripeptides -- BTG
Anti-ganglioside GD2 antibody-interleukin-2 fusion protein -- Lexigen
Anti-GM2 MAb -- Kyowa
Anti-GM-CSF receptor monoclonal antibodies -- AMRAD
Anti-gp130 MAb -- Tosoh
Anti-HCA monoclonal antibodies -- AltaRex/Epigen
Anti-hCG antibodies -- Abgenix/AVI BioPharma
Anti-heparanase human monoclonal antibodies -- Oxford Glycosciences/Medarex
Anti-hepatitis C virus human monoclonal antibodies -- XTL Biopharmaceuticals
Anti-HER-2 antibody gene therapy
Anti-herpes antibody -- Epicyte
Anti-HIV antibody -- Epicyte
anti-HIV catalytic antibody – Hesed Biomed
anti-HIV fusion protein -- Idun
anti-HIV proteins -- Cangene
Anti-HM1-24 MAb -- Chugai
Anti-hR3 MAb
Anti-Human-Carcinoma-Antigen MAb -- Epicyte
Anti-ICAM-1 MAb -- Boehringer Ingelheim
Anti-ICAM-1 MAb 1A-29 -- Pharmacia
Anti-ICAM-1 MAb HA58
Anti-ICAM-1 MAb YN1/1.7.4
Anti-ICAM-3 MAb ICM3 -- ICOS
Anti-idiotype breast cancer vaccine 11D10
Anti-idiotype breast cancer vaccine ACA14C5 –
Anti-idiotype cancer vaccine -- ImClone Systems/Merck KGaA ImClone, Viventia Biotech
Anti-idiotype cancer vaccine 1A7 -- Titan
Anti-idiotype cancer vaccine 3H1 -- Titan
Anti-idiotype cancer vaccine TriAb -- Titan
Anti-idiotype Chlamydia trachomatis vaccine
Anti-idiotype colorectal cancer vaccine -- Novartis
Anti-idiotype colorectal cancer vaccine -- Onyvax
Anti-idiotype melanoma vaccine -- IDEC Pharmaceuticals
Anti-idiotype ovarian cancer vaccine ACA 125
Anti-idiotype ovarian cancer vaccine AR54 -- AltaRex
Anti-idiotype ovarian cancer vaccine CA-125 – AltaRex, Biomira
Anti-IgE catalytic antibody -- Hesed Biomed
Anti-IgE MAb E26 -- Genentech
Anti-IGF-1 MAb
anti-inflammatory – GeneMax
anti-inflammatory peptide -- BTG

FIG. 1D

anti-integrin peptides -- Burnha
Anti-interferon-alpha-receptor MAb 64G12 -- Pharma Pacific Management
Anti-interferon-gamma MAb -- Protein Design Labs
Anti-interferon-gamma polyclonal antibody -- Advanced Biotherapy
Anti-interleukin-10 MAb --
Anti-interleukin-12 MAb –
Anti-interleukin-1-beta polyclonal antibody -- R&D Systems
Anti-interleukin-2 receptor MAb 2A3
Anti-interleukin-2 receptor MAb 33B3-1 -- Immunotech
Anti-interleukin-2 receptor MAb ART-18
Anti-interleukin-2 receptor MAb LO-Tact-1
Anti-interleukin-2 receptor MAb Mikbeta1
Anti-interleukin-2 receptor MAb NDS61
Anti-interleukin-4 MAb 11B11
Anti-interleukin-5 MAb -- Wallace Laboratories
Anti-interleukin-6 MAb – Centocor, Diaclone, Pharmadigm
Anti-interleukin-8 MAb -- Xenotech
Anti-JL1 MAb
Anti-Klebsiella sheep MAb -- KS Biomedix Holdings
Anti-Laminin receptor MAb-liposomal doxorubicin conjugate
Anti-LCG MAb -- Cytoclonal
Anti-lipopolysaccharide MAb -- VitaResc
Anti-L-selectin monoclonal antibodies -- Protein Design Labs, Abgenix, Stanford University
Anti-MBL monoclonal antibodies -- Alexion/Brigham and Women's Hospital
Anti-MHC monoclonal antibodies
Anti-MIF antibody humanised – IDEC, Cytokine PharmaSciences
Anti-MRSA/VRSA sheep MAb -- KS Biomedix Holdings
Anti-mu MAb -- Novartis
Anti-MUC-1 MAb
Anti-Nogo-A MAb IN1
Anti-nuclear autoantibodies -- Procyon
Anti-ovarian cancer monoclonal antibodies -- Dompe
Anti-p185 monoclonal antibodies
Anti-p43 MAb
Antiparasitic vaccines
Anti-PDGF/bFGF sheep MAb -- KS Biomedix
Anti-properdin monoclonal antibodies -- Abgenix/Gliatech
Anti-PSMA MAb J591 -- BZL Biologics
Anti-Rev MAb gene therapy –
Anti-RSV antibodies – Epicyte, Intracell
Anti-RSV monoclonal antibodies -- Medarex/MedImmune, Applied Molecular Evolution/MedImmune
Anti-RSV MAb, inhalation -- Alkermes/MedImmune
Anti-RT gene therapy
Antisense K-ras RNA gene therapy
Anti-SF-25 MAb
Anti-sperm antibody -- Epicyte
Anti-Tac(Fv)-PE38 conjugate
Anti-TAPA/CD81 MAb AMP1
Anti-tat gene therapy
Anti-TCR-alphabeta MAb H57-597
Anti-TCR-alphabeta MAb R73
Anti-tenascin MAb BC-4-I-131
Anti-TGF-beta human monoclonal antibodies -- Cambridge Antibody Tech., Genzyme
Anti-TGF-beta MAb 2G7 -- Genentech
Antithrombin III -- Genzyme Transgenics, Aventis, Bayer, Behringwerke, CSL, Myriad
Anti-Thy1 MAb
Anti-Thy1.1 MAb

FIG. 1E

Anti-tissue factor/factor VIIA sheep MAb -- KS Biomedix
Anti-TNF monoclonal antibodies -- Centocor, Chiron, Peptech, Pharacia, Serono
Anti-TNF sheep MAb -- KS Biomedix Holdings
Anti-TNFalpha MAb -- Genzyme
Anti-TNFalpha MAb B-C7 -- Diaclone
Anti-tooth decay MAb -- Planet BioTech.
antitumour RNases -- NIH
Anti-VCAM MAb 2A2 -- Alexion
Anti-VCAM MAb 3F4 -- Alexion
Anti-VCAM-1 MAb
Anti-VEC MAb -- ImClone
Anti-VEGF MAb -- Genentech
Anti-VEGF MAb 2C3
Anti-VEGF sheep MAb -- KS Biomedix Holdings
Anti-VLA-4 MAb HP1/2 -- Biogen
Anti-VLA-4 MAb PS/2
Anti-VLA-4 MAb R1-2
Anti-VLA-4 MAb TA-2
Anti-VRE sheep MAb -- KS Biomedix Holdings
ANUP -- TranXenoGen
ANUP-1 -- Pharis
AOP-RANTES -- Senetek
Apan-CH -- Praecis Pharmaceuticals
APC-8024 -- Demegen
ApoA-1 -- Milano, Pharmacia
Apogen -- Alexion
apolipoprotein A1 -- Avanir
Apolipoprotein E -- Bio-Tech. General
Applaggin -- Biogen
aprotinin -- ProdiGene
APT-070C -- AdProTech
AR 177 -- Aronex Pharmaceuticals
AR 209 -- Aronex Pharmaceuticals, Antigenics
AR545C
ARGENT gene delivery systems -- ARIAD
Arresten
ART-123 -- Asahi Kasei
arylsulfatase B -- BioMarin
Arylsulfatase B, Recombinant human -- BioMarin
AS 1051 -- Ajinomoto
ASI-BCL -- Intracell
ATL-101 -- Alizyme
atrial natriuretic peptide -- Pharis
Aurintricarboxylic acid-high molecular weight
autoimmune disorders -- GPC Biotech/MorphoSys
Autoimmune disorders and transplant rejection -- Bristol-Myers Squibb/Genzyme Tra
Autoimmune disorders/cancer -- Abgenix/Chiron, /CuraGen
Autotaxin
Avicidin -- NeoRx
axogenesis factor-1 -- Boston Life Sciences
Axokine -- Regeneron
B cell lymphoma vaccine -- Biomira
B7-1 gene therapy --
BABS proteins -- Chiron
BAM-002 -- Novelos Therapeutics
Bay-16-9996 -- Bayer
Bay-39-9437 -- Bayer
Bay-50-4798 -- Bayer
BB-10153 -- British Biotech
BBT-001 -- Bolder BioTech.
BBT-002 -- Bolder BioTech.
BBT-003 -- Bolder BioTech.
BBT-004 -- Bolder BioTech.
BBT-005 -- Bolder BioTech.
BBT-006 -- Bolder BioTech.
BBT-007 -- Bolder BioTech.
BCH-2763 -- Shire
BCSF -- Millenium Biologix
BDNF -- Regeneron -- Amgen

FIG. 1F

Becaplermin -- Johnson & Johnson, Chiron
Bectumomab – Immunomedics
Beta-adrenergic receptor gene therapy -- University of Arkansas
BI 51013 -- Behringwerke AG
BIBH 1 -- Boehringer Ingelheim
BIM-23190 -- Beaufour-Ipsen
birch pollen immunotherapy -- Pharmacia
bispecific fusion proteins -- NIH
Bispecific MAb 2B1 -- Chiron
Bitistatin
BIWA 4 -- Boehringer Ingelheim
blood substitute – Northfield, Baxter Intl.
BLP-25 -- Biomira
BLS-0597 -- Boston Life Sciences
BLyS -- Human Genome Sciences
BLyS radiolabelled -- Human Genome Sciences
BM 06021 -- Boehringer Mannheim
BM-202 -- BioMarin
BM-301 -- BioMarin
BM-301 -- BioMarin
BM-302 -- BioMarin
BMP 2 -- Genetics Institute/Medtronic-Sofamor Danek, Genetics Institute/ Collagenesis, Genetics Institute/Yamanouch
BMP 2 gene therapy
BMP 52 -- Aventis Pasteur, Biopharm
BMP-2 -- Genetics Institute
BMS 182248 -- Bristol-Myers Squibb
BMS 202448 -- Bristol-Myers Squibb
bone growth factors -- IsoTis
BPC-15 -- Pfizer
brain natriuretic peptide –
Breast cancer -- Oxford GlycoSciences/Medarex
Breast cancer vaccine -- Therion Biologics, Oregon
BSSL -- PPL Therapeutics
BST-2001 – BioStratum
BST-3002 -- BioStratum
BTI 322 –
butyrylcholinesterase -- Shire
C 6822 -- COR Therapeutics
C1 esterase inhibitor -- Pharming
C3d adjuvant -- AdProTech
CAB-2.1 -- Millennium
calcitonin – Inhale Therapeutics Systems, Aventis, Genetronics, TranXenoGen, Unigene, Rhone Poulenc Rohrer
calcitonin -- oral – Nobex, Emisphere, Pharmaceutical Discovery
Calcitonin gene-related peptide -- Asahi Kasei -- Unigene
calcitonin, human -- Suntory
calcitonin, nasal – Novartis, Unigene
calcitonin, Panoderm -- Elan
calcitonin, Peptitrol -- Shire
calcitonin, salmon -- Therapicon
calin -- Biopharm
Calphobindin I
calphobindin I -- Kowa
calreticulin -- NYU
Campath-1G
Campath-1M
cancer therapy -- Cangene
cancer vaccine – Aixlie, Aventis Pasteur, Center of Molecular Immunology ,YM BioSciences, Cytos, Genzyme, Transgenics, GlobeImmune, Igeneon, ImClone, Virogenetics, InterCell, Iomai, Jenner Biotherapies, Memorial Sloan-Kettering Cancer Center, Sydney Kimmel Cancer Center, Novavax, Protein Sciences, Argonex, SIGA
Cancer vaccine ALVAC-CEA B7.1 -- Aventis Pasteur/Therion Biologics
Cancer vaccine CEA-TRICOM -- Aventis Pasteur/Therion Biologics
Cancer vaccine gene therapy -- Cantab Pharmaceuticals

FIG. 1G

Cancer vaccine HER-2/neu -- Corixa
Cancer vaccine THERATOPE -- Biomira
cancer vaccine, PolyMASC -- Valentis
Candida vaccine – Corixa, Inhibitex
Canstatin -- ILEX
CAP-18 -- Panorama
Cardiovascular gene therapy -- Collateral Therapeutics
carperitide -- Suntory
Casocidin-1 -- Pharis
CAT 152 -- Cambridge Antibody Tech.
CAT 192 -- Cambridge Antibody Tech.
CAT 213 -- Cambridge Antibody Tech.
Catalase-- Enzon
Cat-PAD -- Circassia
CB 0006 -- Celltech
CCK(27-32)-- Akzo Nobel
CCR2-64I -- NIH
CD, Procept -- Paligent
CD154 gene therapy
CD39 -- Immunex
CD39-L2 -- Hyseq
CD39-L4 -- Hyseq
CD4 fusion toxin -- Senetek
CD4 IgG -- Genentech
CD4 receptor antagonists -- Pharmacopeia/Progenics
CD4 soluble -- Progenics
CD4, soluble -- Genzyme Transgenics
CD40 ligand -- Immunex
CD4-ricin chain A -- Genentech
CD59 gene therapy -- Alexion
CD8 TIL cell therapy -- Aventis Pasteur
CD8, soluble -- Avidex
CD95 ligand -- Roche
CDP 571 -- Celltech
CDP 850 -- Celltech
CDP 870 -- Celltech
CDS-1 -- Ernest Orlando
Cedelizumab -- Ortho-McNeil
Cetermin -- Insmed
CETP vaccine -- Avant
Cetrorelix
Cetuximab
CGH 400 -- Novartis
CGP 42934 -- Novartis
CGP 51901 – Tanox
CGRP -- Unigene
CGS 27913 -- Novartis
CGS 32359 -- Novartis
Chagas disease vaccine -- Corixa
chemokines -- Immune Response
CHH 380 -- Novartis
chitinase – Genzyme, ICOS
Chlamydia pneumoniae vaccine -- Antex Biologics
Chlamydia trachomatis vaccine -- Antex Biologics
Chlamydia vaccine -- GlaxoSmithKline
Cholera vaccine CVD 103-HgR -- Swiss Serum and Vaccine Institute Berne
Cholera vaccine CVD 112 -- Swiss Serum and Vaccine Institute Berne
Cholera vaccine inactivated oral -- SBL Vaccin
Chrysalin -- Chrysalis BioTech.
CI-782 -- Hitachi Kase
Ciliary neurotrophic factor – Fidia, Roche
CIM project -- Active Biotech
CL 329753 -- Wyeth-Ayerst
CL22, Cobra -- ML Laboratories
Clenoliximab -- IDEC
Clostridium difficile antibodies -- Epicyte
clotting factors -- Octagene
CMB 401 -- Celltech
CNTF -- Sigma-Tau
Cocaine abuse vaccine – Cantab, ImmuLogic, Scripps
coccidiomycosis vaccine -- Arizo
collagen -- Type I -- Pharming
Collagen formation inhibitors -- FibroGen

FIG. 1H

Collagen/hydroxyapatite/bone growth factor -- Aventis Pasteur, Biopharm, Orquest
collagenase -- BioSpecifics
Colorectal cancer vaccine -- Wistar Institute
Component B, Recombinant -- Serono
Connective tissue growth factor inhibitors -- FibroGen/Taisho
Contortrostatin
contraceptive vaccine -- Zonagen
Contraceptive vaccine hCG
Contraceptive vaccine male reversible -- IMMUCON
Contraceptive vaccine zona pellucida -- Zonagen
Copper-64 labelled MAb TETA-1A3 -- NCI
Coralyne
Corsevin M
C-peptide analogues -- Schwarz
CPI-1500 -- Consensus
CRF -- Neurobiological Tech.
cRGDfV pentapeptide --
CRL 1095 -- CytRx
CRL 1336 -- CytRx
CRL 1605 -- CytRx
CS-560 -- Sankyo
CSF -- ZymoGenetics
CSF-G -- Hangzhou, Dong-A, Hanmi
CSF-GM -- Cangene, Hunan, LG Chem
CSF-M -- Zarix
CT 1579 -- Merck Frosst
CT 1786 -- Merck Frosst
CT-112^ -- BTG
CTB-134L -- Xenova
CTC-111 -- Kaketsuken
CTGF -- FibroGen
CTLA4-Ig -- Bristol-Myers Squibb
CTLA4-Ig gene therapy --
CTP-37 -- AVI BioPharma
C-type natriuretic peptide -- Suntory
CVS 995 -- Corvas Intl.
CX 397 -- Nikko Kyodo
CY 1747 -- Epimmune
CY 1748 -- Epimmune
Cyanovirin-N
Cystic fibrosis therapy -- CBR/IVAX
CYT 351
cytokine Traps -- Regeneron
cytokines -- Enzon, Cytoclonal
Cytomegalovirus glycoprotein vaccine -- Chiron, Aquila Biopharmaceuticals, Aventis Pasteur, Virogenetics
Cytomegalovirus vaccine live -- Aventis Pasteur
Cytosine deaminase gene therapy -- GlaxoSmithKline
DA-3003 -- Dong-A
DAB389interleukin-6 -- Senetek
DAB389interleukin-7
DAMP^ -- Incyte Genomics
Daniplestim -- Pharmacia
darbepoetin alfa -- Amgen
DBI-3019 -- Diabetogen
DCC -- Genzyme
DDF -- Hyseq
decorin -- Integra, Telios
defensins -- Large Scale Biology
DEGR-VIIa
DeImmunised antibody 3B6/22 AGEN
Deimmunised anti-cancer antibodies -- Biovation/Viragen
Dendroamide A
Dengue vaccine -- Bavarian Nordic, Merck
denileukin diftitox -- Ligand
DES-1101 -- Desmos
desirudin -- Novartis
desmopressin -- Unigene
Desmoteplase -- Merck, Schering AG
Destabilase
Diabetes gene therapy -- DeveloGen, Pfizer
Diabetes therapy -- Crucell
Diabetes type 1 vaccine -- Diamyd Therapeutics

FIG. 1I

DiaCIM -- YM BioSciences
dialytic oligopeptides -- Research Corp
Diamyd -- Diamyd Therapeutics
DiaPep227-- Pepgen
DiavaX -- Corixa
Diphtheria tetanus pertussis-hepatitis B vaccine -- GlaxoSmithKline
DIR therapy -- Solis Therapeutics –
DNase -- Genentech
Dornase alfa -- Genentech
Dornase alfa, inhalation -- Genentech
Doxorubicin-anti-CEA MAb conjugate – Immunomedics
DP-107 -- Trimeris
drotrecogin alfa -- Eli Lilly
DTctGMCSF
DTP-polio vaccine -- Aventis Pasteur
DU 257-KM231 antibody conjugate -- Kyowa
dural graft matrix -- Integra
Duteplase – Baxter Intl.
DWP-401 -- Daewoong
DWP-404 -- Daewoong
DWP-408 -- Daewoong
E coli O157 vaccine -- NIH
E21-R -- BresaGen
Eastern equine encephalitis virus vaccine –
Echicetin –
Echinhibin 1 –
Echistatin -- Merck
Echitamine –
EC-SOD -- PPL Therapeutics
EDF -- Ajinomoto
EDN derivative -- NIH
EDNA -- NIH
Edobacomab -- XOMA
Edrecolomab -- Centocor
EF 5077
Efalizumab -- Genentech
EGF fusion toxin – Seragen, Ligand
EGF-P64k vaccine -- Center of Molecular Immunology
EL 246 -- LigoCyte
elastase inhibitor -- Synergen
elcatonin -- Therapicon
EMD 72000 -- Merck KGaA
Emdogain -- BIORA
emfilermin -- AMRAD
Emoctakin -- Novartis
enamel matrix protein -- BIORA
Endo III -- NYU
endostatin – EntreMed, Pharis
Enhancins -- Micrologix
Enlimomab -- Isis Pharm.
Enoxaparin sodium -- Pharmuka
enzyme linked antibody nutrient depletion therapy -- KS Biomedix Holdings
Eosinophil-derived neutralizing agent –
EP-51216 -- Asta Medica
EP-51389 -- Asta Medica
EPH family ligands -- Regeneron
Epidermal growth factor -- Hitachi Kasei, Johnson & Johnson
Epidermal growth factor fusion toxin -- Senetek
Epidermal growth factor-genistein –
EPI-HNE-4 -- Dyax
EPI-KAL2 -- Dyax
Epoetin-alfa – Amgen, Dragon Pharmaceuticals, Nanjing Huaxin
Epratuzumab – Immunomedics
Epstein-Barr virus vaccine -- Aviron/SmithKline Beecham, Bioresearch
Eptacog alfa -- Novo Nordisk
Eptifibatide -- COR Therapeutics
erb-38 –
Erlizumab -- Genentech

FIG. 1J

erythropoietin -- Alkermes, ProLease, Dong-A, Elanex, Genetics Institute, LG Chem, Protein Sciences, Serono, Snow Brand, SRC VB VECTOR, Transkaryotic Therapies
Erythropoietin Beta -- Hoffman La Roche
Erythropoietin/Epoetin alfa -- Chugai
Escherichia coli vaccine -- North American Vaccine, SBL Vaccin, Swiss Serum and Vaccine Institute Berne
etanercept -- Immunex
examorelin -- Mediolanum
exonuclease VII
F 105 -- Centocor
F-992 -- Fornix
Factor IX -- Alpha Therapeutics, Welfide Corp., CSL, enetics Institute/AHP, Pharmacia, PPL Therapeutics
Factor IX gene therapy -- Cell Genesys
Factor VII -- Novo Nordisk, Bayer, Baxter Intl.
Factor VIIa -- PPL Therapeutics, ZymoGenetics
Factor VIII -- Bayer Genentech, Beaufour-Ipsen, CLB, Inex, Octagen, Pharmacia, Pharming
Factor VIII -- PEGylated -- Bayer
Factor VIII fragments -- Pharmacia
Factor VIII gene therapy -- Targeted Genetics
Factor VIII sucrose formulation -- Bayer, Genentech
Factor VIII-2 -- Bayer
Factor VIII-3 -- Bayer
Factor Xa inhibitors -- Merck, Novo Nordisk, Mochida
Factor XIII -- ZymoGenetics
Factors VIII and IX gene therapy -- Genetics Institute/Targeted Genetics
Famoxin -- Genset
Fas (delta) TM protein -- LXR BioTech.
Fas TR -- Human Genome Sciences
Felvizumab -- Scotgen
FFR-VIIa -- Novo Nordisk
FG-001 -- F-Gene
FG-002 -- F-Gene
FG-004 -- F-Gene
FG-005 -- F-Gene
FGF + fibrin -- Repair
Fibrimage -- Bio-Tech. General
fibrin-binding peptides -- ISIS Innovation
fibrinogen -- PPL Therapeutics, Pharming
fibroblast growth factor -- Chiron, NYU, Ramot, ZymoGenetics
fibrolase conjugate -- Schering AG
Filgrastim -- Amgen
filgrastim -- PDA modified -- Xencor
FLT-3 ligand -- Immunex
FN18 CRM9 --
follistatin -- Biotech Australia, Human Therapeutics
follitropin alfa -- Alkermes, ProLease, PowderJect, Serono, Akzo Nobel
Follitropin Beta -- Bayer, Organon
FP 59
FSH -- Ferring
FSH + LH -- Ferring
F-spondin -- CeNeS
fusion protein delivery system -- UAB Research Foundation
fusion toxins -- Boston Life Sciences
G 5598 -- Genentech
GA-II -- Transkaryotic Therapies
Gamma-interferon analogues -- SRC VB VECTOR
Ganirelix -- Roche
gastric lipase -- Meristem
Gavilimomab --
G-CSF -- Amgen, SRC VB VECTOR
GDF-1 -- CeNeS
GDF-5 -- Biopharm
GDNF -- Amgen

FIG. 1K

gelsolin -- Biogen
Gemtuzumab ozogamicin -- Celltech
Gene-activated epoetin-alfa -- Aventis Pharma -- Transkaryotic Therapies
Glanzmann thrombasthenia gene therapy –
Glatiramer acetate -- Yeda
glial growth factor 2 -- CeNeS
GLP-1 – Amylin, Suntory, TheraTech, Watson
GLP-1 peptide analogues – Zealand Pharaceuticals
glucagon -- Eli Lilly, ZymoGenetics
Glucagon-like peptide-1 7-36 amide -- Suntory
Glucocerebrosidase -- Genzyme
glutamate decarboxylase -- Genzyme Transgenics
Glycoprotein S3 -- Kureha
GM-CSF -- Immunex
GM-CSF tumour vaccine -- PowderJect
GnRH immunotherapeutic -- Protherics
gp75 antigen -- ImClone
gp96 -- Antigenics
GPI 0100 -- Galenica
GR 4991W93 -- GlaxoSmithKline
Granulocyte colony-stimulating factor -- Dong-A
Granulocyte colony-stimulating factor conjugate
grass allergy therapy -- Dynavax
GRF1-44 -- ICN
Growth Factor – Chiron, Atrigel, Atrix, Innogenetics, ZymoGenetics, Novo
growth factor peptides -- Biotherapeutics
growth hormone – LG Chem
growth hormone, Recombinant human -- Serono
GT 4086 -- Gliatech
GW 353430 -- GlaxoSmithKline
GW-278884 -- GlaxoSmithKline
H 11 -- Viventia Biotech
H5N1 influenza A virus vaccine -- Protein Sciences
haemoglobin -- Biopure
haemoglobin 3011, Recombinant -- Baxter Healthcare
haemoglobin crosfumaril – Baxter Intl.
haemoglobin stabilized -- Ajinomoto
haemoglobin, recombinant -- Apex
HAF -- Immune Response
Hantavirus vaccine
HB 19
HBNF -- Regeneron
HCC-1 -- Pharis
hCG -- Milkhaus
hCG vaccine -- Zonagen
HE-317 -- Hollis-Eden Pharmaceuticals
Heat shock protein cancer and influenza vaccines -- StressGen
Helicobacter pylori vaccine -- Acambis, AstraZeneca/CSL, Chiron, Provalis
Helistat-G -- GalaGen
Hemolink -- Hemosol
hepapoietin -- Snow Brand
heparanase -- InSight
heparinase I -- Ibex
heparinase III -- Ibex
Hepatitis A vaccine -- American Biogenetic Sciences
Hepatitis A vaccine inactivated
Hepatitis A vaccine Nothav -- Chiron
Hepatitis A-hepatitis B vaccine -- GlaxoSmithKline
hepatitis B therapy -- Tripep
Hepatitis B vaccine – Amgen, Chiron SpA, Meiji Milk, NIS, Prodeva, PowderJect, Rhein Biotech
Hepatitis B vaccine recombinant -- Evans Vaccines, Epitec Combiotech, Genentech, MedImmune, Merck Sharp & Dohme, Rhein Biotech, Shantha Biotechnics, Vector, Yeda

FIG. 1L

Hepatitis B vaccine recombinant TGP 943 -- Takeda
Hepatitis C vaccine -- Bavarian Nordic, Chiron, Innogenetics Acambis,
Hepatitis D vaccine -- Chiron Vaccines
Hepatitis E vaccine recombinant -- Genelabs/GlaxoSmithKline, Novavax
hepatocyte growth factor – Panorama, Sosei
hepatocyte growth factor kringle fragments -- EntreMed
Her-2/Neu peptides -- Corixa
Herpes simplex glycoprotein DNA vaccine – Merck, Wyeth-Lederle Vaccines-Malvern, Genentech, GlaxoSmithKline, Chiron, Takeda
Herpes simplex vaccine -- Cantab Pharmaceuticals, CEL-SCI, Henderson Morley
Herpes simplex vaccine live -- ImClone Systems/Wyeth-Lederle, Aventis Pasteur
HGF derivatives -- Dompe
hIAPP vaccine -- Crucell
Hib-hepatitis B vaccine -- Aventis Pasteur
HIC 1
HIP-- Altachem
Hirudins – Biopharma, Cangene, Dongkook, Japan Energy Corporation, Pharmacia Corporation, SIR International, Sanofi-Synthelabo, Sotragene, Rhein Biotech
HIV edible vaccine -- ProdiGene
HIV gp120 vaccine – Chiron, Ajinomoto, GlaxoSmithKline, ID Vaccine, Progenics, VaxGen
HIV gp120 vaccine gene therapy –
HIV gp160 DNA vaccine – PowderJect, Aventis Pasteur, Oncogen, Hyland Immuno, Protein Sciences
HIV gp41 vaccine -- Panacos
HIV HGP-30W vaccine -- CEL-SCI
HIV immune globulin – Abbott, Chiron
HIV peptides -- American Home Products
HIV vaccine -- Applied bioTech., Axis Genetics, Biogen, Bristol-Myers Squibb, Genentech, Korea Green Cross, NIS, Oncogen, Protein Sciences Corporation, Terumo, Tonen Corporation, Wyeth-Ayerst, Wyeth-Lederle Vaccines-Malvern, Advanced BioScience Laboratories, Bavarian Nordic, Bavarian Nordic/Statens Serum Institute, GeneCure, Immune Response, Progenics, Therion Biologics, United Biomedical, Chiron
HIV vaccine vCP1433 -- Aventis Pasteur
HIV vaccine vCP1452 -- Aventis Pasteur
HIV vaccine vCP205 -- Aventis Pasteur
HL-9 -- American BioScience
HM-9239 -- Cytran
HML-103 -- Hemosol
HML-104 -- Hemosol
HML-105 -- Hemosol
HML-109 -- Hemosol
HML-110 -- Hemosol
HML-121 -- Hemosol
hNLP -- Pharis
Hookworm vaccine
host-vector vaccines – Henogen
HPM 1 -- Chugai
HPV vaccine -- MediGene
HSA -- Meristem
HSF – StressGen
HSP carriers –Weizmann, Yeda, Peptor
HSPPC-70 -- Antigenics
HSPPC-96 -- pathogen-derived -- Antigenics
HSV 863 -- Novartis
HTLV-I DNA vaccine
HTLV-I vaccine
HTLV-II vaccine -- Access
HU 901 -- Tanox
Hu23F2G -- ICOS
HuHMFG1

FIG. 1M

HumaLYM -- Intracell
Human krebs statika -- Yamanouchi
human monoclonal antibodies -- Abgenix/Biogen, Abgenix/ Corixa, Abgenix/Immunex, Abgenix/Lexicon, Abgenix/ Pfizer, Athersys/Medarex, Biogen/MorphoSys, CAT/Searle, Centocor/Medarex, Corixa/Kirin Brewery, Corixa/Medarex, Eos BioTech./Medarex, Eos/Xenerex, Exelixis/Protein Design Labs, ImmunoGen/ Raven, Medarex/B.Twelve, MorphoSys/ImmunoGen, XTL Biopharmaceuticals/Dyax,
Human monoclonal antibodies -- Medarex/Northwest Biotherapeutics, Medarex/Seattle Genetics
human netrin-1 -- Exelixis
human papillomavirus antibodies -- Epicyte
Human papillomavirus vaccine -- Biotech Australia, IDEC, StressGen
Human papillomavirus vaccine MEDI 501 -- MedImmune/GlaxoSmithKline
Human papillomavirus vaccine MEDI 503/MEDI 504 -- MedImmune/GlaxoSmithKline
Human papillomavirus vaccine TA-CIN -- Cantab Pharmaceuticals
Human papillomavirus vaccine TA-HPV -- Cantab Pharmaceuticals
Human papillomavirus vaccine TH-GW -- Cantab/GlaxoSmithKline
human polyclonal antibodies -- Biosite/Eos BioTech./ Medarex
human type II anti factor VIII monoclonal antibodies -- ThromboGenics
humanised anti glycoprotein Ib murine monoclonal antibodies -- ThromboGenics
HumaRAD -- Intracell
HuMax EGFR -- Genmab
HuMax-CD4 -- Medarex
HuMax-IL15 -- Genmab
HYB 190 -- Hybridon
HYB 676 -- Hybridon
I-125 MAb A33 -- Celltech
Ibritumomab tiuxetan -- IDEC
IBT-9401 -- Ibex
IBT-9402 -- Ibex
IC 14 -- ICOS
Idarubicin anti-Ly-2.1 –
IDEC 114 -- IDEC
IDEC 131 -- IDEC
IDEC 152 -- IDEC
IDM 1 -- IDM
IDPS -- Hollis-Eden Pharmaceuticals
iduronate-2-sulfatase -- Transkaryotic Therapies
IGF/IBP-2-13 -- Pharis
IGN-101 -- Igeneon
IK HIR02 -- Iketon
IL-11 -- Genetics Institute/AHP
IL-13-PE38 -- NeoPharm
IL-17 receptor -- Immunex
IL-18BP -- Yeda
IL-1Hy1 -- Hyseq
IL-1ß -- Celltech
IL-1ß adjuvant -- Celltech
IL-2 -- Chiron
IL-2 + IL-12 -- Hoffman La-Roche
IL-6/sIL-6R fusion -- Hadasit
IL-6R derivative -- Tosoh
IL-7-Dap 389 fusion toxin -- Ligand
IM-862 -- Cytran
IMC-1C11 -- ImClone
imiglucerase -- Genzyme
Immune globulin intravenous (human) -- Hoffman La Roche
immune privilege factor -- Proneuron
Immunocal -- Immunotec
Immunogene therapy -- Briana Bio-Tech
Immunoliposomal 5-fluorodeoxyuridine-dipalmitate –

FIG. 1N

immunosuppressant vaccine -- Aixlie
immunotoxin – Antisoma, NIH
ImmuRAIT-Re-188 – Immunomedics
imreg-1 -- Imreg
infertility -- Johnson & Johnson, E-TRANS
Influenza virus vaccine -- Aventis Pasteur, Protein Sciences
inhibin -- Biotech Australia, Human Therapeutics
Inhibitory G protein gene therapy
INKP-2001 -- InKine
Inolimomab -- Diaclone
insulin -- AutoImmune, Altea, Biobras, BioSante, Bio-Tech. General, Chong Kun Dang, Emisphere, Flamel, Provalis, Rhein Biotech, TranXenoGen
insulin (bovine) -- Novartis
insulin analogue -- Eli Lilly
Insulin Aspart -- Novo Nordisk
insulin detemir -- Novo Nordisk
insulin glargine -- Aventis
insulin inhaled – Inhale Therapeutics Systems, Alkermes
insulin oral -- Inovax
insulin, AeroDose -- AeroGen
insulin, AERx -- Aradigm
insulin, BEODAS -- Elan
insulin, Biphasix -- Helix
insulin, buccal -- Generex
insulin, I2R -- Flemington
insulin, intranasal -- Bentley
insulin, oral – Nobex, Unigene
insulin, Orasome -- Endorex
insulin, ProMaxx -- Epic
insulin, Quadrant -- Elan
insulin, recombinant -- Aventis
insulin, Spiros -- Elan
insulin, Transfersome -- IDEA
insulin, Zymo, recombinant -- Novo Nordisk
insulinotropin -- Scios
Insulysin gene therapy –

integrin antagonists -- Merck
interferon (Alpha2) -- SRC VB VECTOR, Viragen, Dong-A, Hoffman La-Roche, Genentech
interferon – BioMedicines, Human Genome Sciences
interferon (Alfa-n3)—Interferon Sciences Intl.
interferon (Alpha), Biphasix -- Helix
interferon (Alpha)—Amgen, BioNative, Novartis, Genzyme Transgenics, Hayashibara, Inhale Therapeutics Systems, Medusa, Flamel, Dong-A, GeneTrol, Nastech, Shantha, Wassermann, LG Chem, Sumitomo, Aventis, Behring EGIS, Pepgen, Servier, Rhein Biotech,
interferon (Alpha2A)
interferon (Alpha2B) – Enzon, Schering-Plough, Biogen, IDEA
interferon (Alpha-N1) -- GlaxoSmithKline
interferon (beta) – Rentschler, GeneTrol, Meristem, Rhein Biotech, Toray, Yeda, Daiichi, Mochida
interferon (Beta1A) – Serono, Biogen
interferon (beta1A),inhale -- Biogen
interferon (ß1b)-- Chiron
interferon (tau)-- Pepgen
Interferon alfacon-1 -- Amgen
Interferon alpha-2a vaccine
Interferon Beta 1b -- Schering/Chiron, InterMune
Interferon Gamma -- Boehringer Ingelheim, Sheffield, Rentschler, Hayashibara
interferon receptor , Type I -- Serono
interferon(Gamma1B) -- Genentech
Interferon-alpha-2b + ribavirin – Biogen, ICN
Interferon-alpha-2b gene therapy -- Schering-Plough
Interferon-con1 gene therapy –

FIG. 1O

interleukin-1 antagonists -- Dompe
Interleukin-1 receptor antagonist -- Abbott Bioresearch, Pharmacia
Interleukin-1 receptor type I -- Immunex
interleukin-1 receptor Type II -- Immunex
Interleukin-10 – DNAX, Schering-Plough
Interleukin-10 gene therapy –
interleukin-12 -- Genetics Institute, Hoffman La-Roche
interleukin-13 -- Sanofi
interleukin-13 antagonists -- AMRAD
Interleukin-13-PE38QQR
interleukin-15 -- Immunex
interleukin-16 -- Research Corp
interleukin-18 -- GlaxoSmithKline
Interleukin-1-alpha -- Immunex/Roche
interleukin-2 -- SRC VB VECTOR, Ajinomoto, Biomira
Interleukin-3 -- Cangene
Interleukin-4 -- Immunology Ventures, Sanofi Winthrop, Schering-Plough, Immunex/ Sanofi Winthrop, Bayer, Ono
Interleukin-4 + TNF-Alpha -- NIH
interleukin-4 agonist -- Bayer
interleukin-4 fusion toxin -- Ligand
Interleukin-4 receptor – Immunex, Immun
Interleukin-6 – Ajinomoto, Cangene, Yeda, Genetics Institute, Novartis
interleukin-6 fusion protein –
interleukin-6 fusion toxin – Ligand, Serono
interleukin-7 -- IC Innovations
interleukin-7 receptor -- Immunex
interleukin-8 antagonists -- Kyowa Hakko/Millennium/Pfizer
interleukin-9 antagonists -- Genaera
interleukins -- Cel-Sci
Iodine I 131 tositumomab -- Corixa
ior EPOCIM -- Center of Molecular Immunology
Ior-P3 -- Center of Molecular Immunology
IP-10 -- NIH
IPF -- Metabolex
IR-501 -- Immune Response
ISIS 9125 -- Isis Pharmaceuticals
ISURF No. 1554 -- Millennium
ISURF No. 1866 – Iowa State Univer.
ITF-1697 -- Italfarmaco
IxC 162 -- Ixion
J 695 -- Cambridge Antibody Tech., Genetics Inst., Knoll
Jagged + FGF -- Repair
JKC-362 -- Phoenix Pharmaceuticals
JTP-2942 – Japan Tobacce
Juman monoclonal antibodies -- Medarex/Raven
K02 -- Axys Pharmaceuticals
Keliximab -- IDEC
Keyhole limpet haemocyanin
KGF -- Amgen
KM 871 -- Kyowa
KPI 135 -- Scios
KPI-022 -- Scios
Kringle 5
KSB 304
KSB-201 -- KS Biomedix
L 696418 -- Merck
L 703801 -- Merck
L1 -- Acorda
L-761191 -- Merck
lactoferrin – Meristem, Pharming, Agennix
lactoferrin cardio -- Pharming
LAG-3 -- Serono
LAIT -- GEMMA
LAK cell cytotoxin -- Arizona
lamellarins -- PharmaMar/University of Malaga
laminin A peptides -- NIH
lanoteplase -- Genetics Institute
laronidase -- BioMarin
Lassa fever vaccine
LCAT -- NIH
LDP 01 -- Millennium

FIG. 1P

LDP 02 -- Millennium
Lecithinized superoxide dismutase -- Seikagaku
LeIF adjuvant -- Corixa
leishmaniasis vaccine -- Corixa
lenercept -- Hoffman La-Roche
Lenograstim – Aventis, Chugai
lepirudin -- Aventis
leptin – Amgen, IC Innovations
Leptin gene therapy -- Chiron Corporation
leptin, 2nd-generation -- Amgen
leridistim -- Pharmacia
leuprolide, ProMaxx -- Epic
leuprorelin, oral -- Unigene
LeuTech -- Papatin
LEX 032 -- SuperGen
LiDEPT -- Novartis
lipase -- Altus Biologics
lipid A vaccine -- EntreMed
lipid-linked anchor Tech. – ICRT, ID Biomedical
liposome-CD4 Tech. -- Sheffield
Listeria monocytogenes vaccine
LMB 1
LMB 7
LMB 9 -- Battelle Memorial Institute, NIH
LM-CD45 -- Cantab Pharmaceuticals
lovastatin -- Merck
LSA-3
LT-ß receptor -- Biogen
lung cancer vaccine -- Corixa
lusupultide -- Scios
L-Vax -- AVAX
LY 355455 -- Eli Lilly
LY 366405 -- Eli Lilly
LY-355101 -- Eli Lilly
Lyme disease DNA vaccine -- Vical/Aventis Pasteur
Lyme disease vaccine -- Aquila Biopharmaceuticals, Aventis, Pasteur, Symbicom, GlaxoSmithKline, Hyland Immuno, MedImmune
Lymphocytic choriomeningitis virus vaccine
lymphoma vaccine – Biomira, Genitope
LYP18
lys plasminogen, recombinant
Lysosomal storage disease gene therapy -- Avigen
lysostaphin -- Nutrition 21
M 23 -- Gruenenthal
M1 monoclonal antibodies -- Acorda Therapeutics
MA 16N7C2 – Corvas Intl.
malaria vaccine -- GlaxoSmithKline, AdProTech, Antigenics, Apovia, Aventis Pasteur, Axis Genetics, Behringwerke, CDCP, Chiron Vaccines, Genzyme Transgenics, Hawaii, MedImmune, NIH, NYU, Oxxon, Roche/Saramane, Biotech Australia, Rx Tech
Malaria vaccine CDC/NIIMALVAC-1
malaria vaccine,multicomponent
mammaglobin -- Corixa
mammastatin -- Biotherapeutics
mannan-binding lectin -- NatImmu
mannan-MUC1 -- Psiron
MAP 30
Marinovir -- Phytera
MARstem -- Maret
MB-015 -- Mochida
MBP -- ImmuLogic
MCI-028 -- Mitsubishi-Tokyo
MCIF -- Human Genome Sciences
MDC -- Advanced BioScience -- Akzo Nobel, ICOS
MDX 11 -- Medarex
MDX 210 -- Medarex
MDX 22 -- Medarex
MDX 22

FIG. 1Q

MDX 240 -- Medarex
MDX 33
MDX 44 -- Medarex
MDX 447 -- Medarex
MDX H210 -- Medarex
MDX RA -- Houston BioTech., Medarex
ME-104 -- Pharmexa
Measles vaccine
Mecasermin -- Cephalon/Chiron, Chiron
MEDI 488 -- MedImmune
MEDI 500
MEDI 507 -- BioTransplant
melanin concentrating hormone -- Neurocrine Biosciences
melanocortins -- OMRF
Melanoma monoclonal antibodies -- Viragen
melanoma vaccine -- GlaxoSmithKline, Akzo Nobel, Avant, Aventis Pasteur, Bavarian Nordic, Biovector, CancerVax, Genzyme Molecular Oncology, Humbolt, ImClone Systems, Memorial, NYU, Oxxon
Melanoma vaccine Magevac -- Therion
memory enhancers -- Scios
meningococcal B vaccine -- Chiron
meningococcal vaccine -- CAMR
Meningococcal vaccine group B conjugate -- North American Vaccine
Meningococcal vaccine group B recombinant -- BioChem Vaccines, Microscience
Meningococcal vaccine group Y conjugate -- North American Vaccine
Meningococcal vaccine groups A B and C conjugate -- North American Vaccine
Mepolizumab -- GlaxoSmithKline
Metastatin – EntreMed, Takeda
Met-CkB7 -- Human Genome Sciences
met-enkephalin -- TNI
METH-1 -- Human Genome Sciences
methioninase -- AntiCancer
Methionine lyase gene therapy -- AntiCancer
Met-RANTES – Genexa Biomedical, Serono
Metreleptin
MGDF -- Kirin
MGV -- Progenics
micrin -- Endocrine
microplasmin -- ThromboGenics
MIF -- Genetics Institute
migration inhibitory factor -- NIH
Mim CD4.1 – Xycte Therapies
mirostipen -- Human Genome Sciences
MK 852 -- Merck
Mobenakin -- NIS
molgramostim -- Genetics Institute, Novartis
monoclonal antibodies -- Abgenix/Celltech, Immusol/ Medarex, Viragen/ Roslin Institute, Cambridge Antibody Tech./Elan
MAb 108 –
MAb 10D5 --
MAb 14.18-interleukin-2 immunocytokine -- Lexigen
MAb 14G2a –
MAb 15A10 –
MAb 170 -- Biomira
MAb 177Lu CC49 --
MAb 17F9
MAb 1D7
MAb 1F7 – Immune Network
MAb 1H10-doxorubicin conjugate
MAb 26-2F
MAb 2A11
MAb 2E1 -- RW Johnson
MAb 2F5
MAb 31.1 -- International BioImmune Systems
MAb 32 -- Cambridge Antibody Tech., Peptech
MAb 323A3 -- Centocor
MAb 3C5

FIG. 1R

MAb 3F12
MAb 3F8
MAb 42/6
MAb 425 -- Merck KGaA
MAb 447-52D -- Merck Sharp & Dohme
MAb 45-2D9- -- haematoporphyrin conjugate
MAb 4B4
MAb 4E3-CPA conjugate -- BCM Oncologia
MAb 4E3-daunorubicin conjugate
MAb 50-6
MAb 50-61A -- Institut Pasteur
MAb 5A8 -- Biogen
MAb 791T/36-methotrexate conjugate
MAb 7c11.e8
MAb 7E11 C5-selenocystamine conjugate
MAb 93KA9 -- Novartis
MAb A5B7-cisplatin conjugate -- Biodynamics Research, Pharmacia
MAb A5B7-I-131
MAb A7
MAb A717 -- Exocell
MAb A7-zinostatin conjugate
MAb ABX-RB2 -- Abgenix
MAb ACA 11
MAb AFP-I-131 – Immunomedics
MAb AP1
MAb AZ1
MAb B3-LysPE40 conjugate
MAb B4 – United Biomedical
MAb B43 Genistein-conjugate
MAb B43.13-Tc-99m -- Biomira
MAb B43-PAP conjugate
MAb B4G7-gelonin conjugate
MAb BCM 43-daunorubicin conjugate -- BCM Oncologia
MAb BIS-1
MAb BMS 181170 -- Bristol-Myers Squibb
MAb BR55-2
MAb BW494
MAb C 242-DM1 conjugate -- ImmunoGen
MAb C242-PE conjugate
MAb c30-6
MAb CA208-cytorhodin-S conjugate -- Hoechst Japan
MAb CC49 -- Enzon
MAb ch14.18 –
MAb CH14.18-GM-CSF fusion protein -- Lexigen
MAb chCE7
MAb CI-137 -- AMRAD
MAb cisplatin conjugate
MAb CLB-CD19
MAb CLB-CD19v
MAb CLL-1 -- Peregrine
MAb CLL-1-GM-CSF conjugate
MAb CLL-1-IL-2 conjugate -- Peregrine
MAb CLN IgG -- doxorubicin conjugates
MAb conjugates – Tanox
MAb D612
MAb Dal B02
MAb DC101 -- ImClone
MAb EA 1 –
MAb EC708 -- Biovation
MAb EP-5C7 -- Protein Design Labs
MAb ERIC-1 -- ICRT
MAb F105 gene therapy
MAb FC 2.15
MAb G250 -- Centocor
MAb GA6
MAb GA733
MAb Gliomab-H -- Viventia Biotech
MAb HB2-saporin conjugate
MAb HD 37 –
MAb HD37-ricin chain-A conjugate
MAb HNK20 -- Acambis
MAb huN901-DM1 conjugate -- ImmunoGen
MAb I-131 CC49 -- Corixa
MAb ICO25
MAb ICR12-CPG2 conjugate
MAb ICR-62

FIG. 1S

MAb IRac-ricin A conjugate
MAb K1
MAb KS1-4-methotrexate conjugate
MAb L6 -- Bristol-Myers Squibb, Oncogen
MAb LiCO 16-88
MAb LL2-I-131 – Immunomedics
MAb LL2-Y-90
MAb LS2D617 -- Hybritech
MAb LYM-1-gelonin conjugate
MAb LYM-1-I-131
MAb LYM-1-Y-90
MAb LYM-2 -- Peregrine
MAb M195
MAb M195-bismuth 213 conjugate -- Protein Design Labs
MAb M195-gelonin conjugate
MAb M195-I-131
MAb M195-Y-90
MAb MA 33H1 -- Sanofi
MAb MAD11
MAb MGb2
MAb MINT5
MAb MK2-23
MAb MOC31 ETA(252-613) conjugate
MAb MOC-31-In-111
MAb MOC-31-PE conjugate
MAb MR6 –
MAb MRK-16 -- Aventis Pasteur
MAb MS11G6
MAb MX-DTPA BrE-3
MAb MY9
MAb Nd2 -- Tosoh
MAb NG-1 -- Hygeia
MAb NM01 – Nissin Food
MAb OC 125
MAb OC 125-CMA conjugate
MAb OKI-1 -- Ortho-McNeil
MAb OX52 -- Bioproducts for Science
MAb PMA5
MAb PR1
MAb prost 30
MAb R-24
MAb R-24 α Human GD3 -- Celltech
MAb RFB4-ricin chain A conjugate
MAb RFT5-ricin chain A conjugate
MAb SC 1
MAb SM-3 -- ICRT
MAb SMART 1D10 -- Protein Design Labs
MAb SMART ABL 364 -- Novartis
MAb SN6f
MAb SN6f-deglycosylated ricin A chain conjugate –
MAb SN6j
MAb SN7-ricin chain A conjugate
MAb T101-Y-90 conjugate -- Hybritech
MAb T-88 -- Chiron
MAb TB94 -- Cancer ImmunoBiology
MAb TEC 11
MAb TES-23 -- Chugai
MAb TM31 -- Avant
MAb TNT-1 -- Cambridge Antibody Tech., Peregrine
MAb TNT-3
MAb TNT-3 -- IL2 fusion protein –
MAb TP3-At-211
MAb TP3-PAP conjugate –
MAb UJ13A -- ICRT
MAb UN3
MAb ZME-018-gelonin conjugate
MAb-BC2 -- GlaxoSmithKline
MAb-DM1 conjugate -- ImmunoGen
MAb-ricin-chain-A conjugate -- XOMA
MAb-temoporfin conjugates
Monopharm C -- Viventia Biotech
monteplase -- Eisai
montirelin hydrate -- Gruenenthal
moroctocog alfa -- Genetics Institute
Moroctocog-alfa -- Pharmacia
MP 4
MP-121 -- Biopharm
MP-52 -- Biopharm
MRA -- Chugai

FIG. 1T

MS 28168 -- Mitsui Chemicals, Nihon Schering
MSH fusion toxin -- Ligand
MSI-99 -- Genaera
MT 201 -- Micromet
Muc-1 vaccine -- Corixa
mucosal tolerance -- Aberdeen
mullerian inhibiting subst
muplestim -- Genetics Institute, Novartis, DSM Anti-Infectives
murine MAb -- KS Biomedix
Mutant somatropin -- JCR Pharmaceutical
MV 833 -- Toagosei
Mycoplasma pulmonis vaccine
Mycoprex -- XOMA
myeloperoxidase -- Henogen
myostatin -- Genetics Institute
Nacolomab tafenatox -- Pharmacia
nagrestipen -- British Biotech
NAP-5 -- Corvas Intl.
NAPc2 -- Corvas Intl.
nartograstim -- Kyowa
Natalizumab -- Protein Design Labs
Nateplase -- NIH, Nihon Schering
nateplase -- Schering AG
NBI-3001 -- Neurocrine Biosci.
NBI-5788 -- Neurocrine Biosci.
NBI-6024 -- Neurocrine Biosci.
Nef inhibitors -- BRI
Neisseria gonorrhoea vaccine -- Antex Biologics
Neomycin B-arginine conjugate
Nerelimomab -- Chiron
Nerve growth factor -- Amgen -- Chiron, Genentech
Nerve growth factor gene therapy
nesiritide citrate -- Scios
neuregulin-2 -- CeNeS
neurocan -- NYU
neuronal delivery system -- CAMR
Neuroprotective vaccine -- University of Auckland
neurotrophic chimaeras -- Regeneron
neurotrophic factor -- NsGene, CereMedix
NeuroVax -- Immune Response
neurturin -- Genentech
neutral endopeptidase -- Genentech
NGF enhancers -- NeuroSearch
NHL vaccine -- Large Scale Biology
NIP45 -- Boston Life Sciences
NKI-B20
NM 01 -- Nissin Food
NMI-139 -- NitroMed
NMMP -- Genetics Institute
NN-2211 -- Novo Nordisk
Noggin -- Regeneron
Nonacog alfa
Norelin -- Biostar
Norwalk virus vaccine
NRLU 10 -- NeoRx
NRLU 10 PE -- NeoRx
NT-3 -- Regeneron
NT-4/5 -- Genentech
NU 3056
NU 3076
NX 1838 -- Gilead Sciences
NY ESO-1/CAG-3 antigen -- NIH
NYVAC-7 -- Aventis Pasteur
NZ-1002 -- Novazyme
obesity therapy -- Nobex
OC 10426 -- Ontogen
OC 144093 -- Ontogen
OCIF -- Sankyo
Oct-43 -- Otsuka
OK PSA - liposomal
OKT3-gamma-1-ala-ala
OM 991
OM 992
Omalizumab -- Genentech
oncoimmunin-L -- NIH
Oncolysin B -- ImmunoGen

FIG. 1U

Oncolysin CD6 -- ImmunoGen
Oncolysin M -- ImmunoGen
Oncolysin S -- ImmunoGen
Oncophage -- Antigenics
Oncostatin M -- Bristol-Myers Squibb
OncoVax-CL -- Jenner Biotherapies
OncoVax-P -- Jenner Biotherapies
onercept -- Yeda
onychomycosis vaccine -- Boehringer Ingelheim
opebecan -- XOMA
opioids -- Arizona
Oprelvekin -- Genetics Institute
Org-33408 b-- Akzo Nobel
Orolip DP -- EpiCept
oryzacystatin
OSA peptides – GenSci Regeneration
osteoblast-cadherin GF -- Pharis
Osteocalcin-thymidine kinase gene therapy
osteogenic protein -- Curis
osteopontin -- OraPharma
osteoporosis peptides – Integra, Telios
osteoprotegerin – Amgen, SnowBrand
otitis media vaccines -- Antex Biologics
ovarian cancer -- University of Alabama
OX40-IgG fusion protein -- Cantab, Xenova
P 246 -- Diatide
P 30 -- Alfacell
p1025 -- Active Biotech
P-113^ -- Demegen
P-16 peptide -- Transition Therapeutics
p43 -- Ramot
P-50 peptide -- Transition Therapeutics
p53 + RAS vaccine -- NIH, NCI
PACAP(1-27) analogue
paediatric vaccines -- Chiron
Pafase -- ICOS
PAGE-4 plasmid DNA -- IDEC
PAI-2 -- Biotech Australia, Human Therapeutics
Palivizumab -- MedImmune
PAM 4 -- Merck
pamiteplase -- Yamanouchi
pancreatin, Minitabs -- Eurand
Pangen -- Fournier
Pantarin – Selective Genetics
Parainfluenza virus vaccine – Pharmacia, Pierre Fabre
paraoxanase -- Esperion
parathyroid hormone – Abiogen, Korea Green Cross
Parathyroid hormone (1-34) -- Chugai/Suntory
Parkinson's disease gene therapy -- Cell Genesys/ Ceregene
Parvovirus vaccine -- MedImmune
PCP-Scan – Immunomedics
PDGF cocktail -- Theratechnologies
peanut allergy therapy -- Dynavax
PEG anti-ICAM MAb -- Boehringer Ingelheim
PEG asparaginase -- Enzon
PEG glucocerebrosidase
PEG hirudin – Knoll
PEG interferon-alpha-2a -- Roche
PEG interferon-alpha-2b + ribavirin – Biogen, Enzon, ICN Pharmaceuticals, Schering-Plough
PEG MAb A5B7 –
Pegacaristim – Amgen -- Kirin Brewery -- ZymoGenetics
Pegaldesleukin -- Research Corp
pegaspargase -- Enzon
pegfilgrastim -- Amgen
PEG-interferon Alpha -- Viragen
PEG-interferon Alpha 2A -- Hoffman La-Roche
PEG-interferon Alpha 2B -- Schering-Plough
PEG-r-hirudin -- Abbott
PEG-uricase -- Mountain View
Pegvisomant – Genentech

FIG. 1V

PEGylated proteins, PolyMASC -- Valentis
PEGylated recombinant native human leptin -- Roche
Pemtumomab
Penetratin -- Cyclacel
Pepscan – Antisoma
peptide G – Peptech, ICRT
peptide vaccine -- NIH ,NCI
Pexelizumab
pexiganan acetate -- Genaera
Pharmaprojects No. 3179 -- NYU
Pharmaprojects No. 3390 -- Ernest Orlando
Pharmaprojects No. 3417 -- Sumitomo
Pharmaprojects No. 3777 -- Acambis
Pharmaprojects No. 4209 -- XOMA
Pharmaprojects No. 4349 – Baxter Intl.
Pharmaprojects No. 4651
Pharmaprojects No. 4915 -- Avanir
Pharmaprojects No. 5156 -- Rhizogenics
Pharmaprojects No. 5200 -- Pfizer
Pharmaprojects No. 5215 -- Origene
Pharmaprojects No. 5216 -- Origene
Pharmaprojects No. 5218 -- Origene
Pharmaprojects No. 5267 -- ML Laboratories
Pharmaprojects No. 5373 -- MorphoSys
Pharmaprojects No. 5493 -- Metabolex
Pharmaprojects No. 5707 -- Genentech
Pharmaprojects No. 5728 -- Autogen
Pharmaprojects No. 5733 -- BioMarin
Pharmaprojects No. 5757 -- NIH
Pharmaprojects No. 5765 -- Gryphon
Pharmaprojects No. 5830 -- AntiCancer
Pharmaprojects No. 5839 -- Dyax
Pharmaprojects No. 5849 -- Johnson & Johnson
Pharmaprojects No. 5860 -- Mitsubishi-Tokyo
Pharmaprojects No. 5869 – Oxford GlycoSciences
Pharmaprojects No. 5883 -- Asahi Brewery
Pharmaprojects No. 5947 -- StressGen
Pharmaprojects No. 5961 -- Theratechnologies
Pharmaprojects No. 5962 -- NIH
Pharmaprojects No. 5966 -- NIH
Pharmaprojects No. 5994 -- Pharming
Pharmaprojects No. 5995 -- Pharming
Pharmaprojects No. 6023 -- IMMUCON
Pharmaprojects No. 6063 -- Cytoclonal
Pharmaprojects No. 6073 -- SIDDCO
Pharmaprojects No. 6115 -- Genzyme
Pharmaprojects No. 6227 -- NIH
Pharmaprojects No. 6230 -- NIH
Pharmaprojects No. 6236 -- NIH
Pharmaprojects No. 6243 -- NIH
Pharmaprojects No. 6244 -- NIH
Pharmaprojects No. 6281 -- Senetek
Pharmaprojects No. 6365 -- NIH
Pharmaprojects No. 6368 -- NIH
Pharmaprojects No. 6373 -- NIH
Pharmaprojects No. 6408 – Pan Pacific
Pharmaprojects No. 6410 -- Athersys
Pharmaprojects No. 6421 – Oxford GlycoSciences
Pharmaprojects No. 6522 -- Maxygen
Pharmaprojects No. 6523 -- Pharis
Pharmaprojects No. 6538 -- Maxygen
Pharmaprojects No. 6554 -- APALEXO
Pharmaprojects No. 6560 -- Ardana
Pharmaprojects No. 6562 -- Bayer
Pharmaprojects No. 6569 -- Eos
Phenoxazine
Phenylase -- Ibex
Pigment epithelium derived factor – plasminogen activator inhibitor-1, recombinant -- DuPont Pharmaceuticals

FIG. 1W

Plasminogen activators -- Abbott Laboratories, American Home Products, Boehringer Mannheim, Chiron Corporation, DuPont Pharmaceuticals, Eli Lilly, Shionogi, Genentech, Genetics Institute, GlaxoSmithKline, Hemispherx Biopharma, Merck & Co, Novartis, Pharmacia Corporation, Wakamoto, Yeda
plasminogen-related peptides -- Bio-Tech. General/MGH
platelet factor 4 -- RepliGen
Platelet-derived growth factor -- Amgen -- ZymoGenetics
plusonermin-- Hayashibara
PMD-2850 -- Protherics
Pneumococcal vaccine -- Antex Biologics, Aventis Pasteur
Pneumococcal vaccine intranasal -- BioChem Vaccines/Biovector
PR1A3
PR-39
pralmorelin -- Kaken
Pretarget-Lymphoma -- NeoRx
Priliximab -- Centocor
PRO 140 -- Progenics
PRO 2000 -- Procept
PRO 367 -- Progenics
PRO 542 -- Progenics
pro-Apo A-I -- Esperion
prolactin -- Genzyme
Prosaptide TX14(A) -- Bio-Tech. General
prostate cancer antbodies -- Immunex, UroCor
prostate cancer antibody therapy -- Genentech/UroGenesys, Genotherapeutics
prostate cancer immunotherapeutics -- The PSMA Development Company
prostate cancer vaccine -- Aventis Pasteur, Zonagen, Corixa, Dendreon, Jenner Biotherapies, Therion Biologics
prostate-specific antigen -- EntreMed
protein A -- RepliGen
protein adhesives -- Enzon
protein C -- Baxter Intl., PPL Therapeutics, ZymoGenetics
protein C activator -- Gilead Sciences
protein kinase R antags -- NIH
protirelin -- Takeda
protocadherin 2 -- Caprion
Pro-urokinase -- Abbott, Bristol-Myers Squibb, Dainippon, Tosoh -- Welfide
P-selectin glycoprotein ligand-1 -- Genetics Institute
pseudomonal infections -- InterMune
Pseudomonas vaccine -- Cytovax
PSGL-Ig -- American Home Products
PSP-94 -- Procyon
PTH 1-34 -- Nobex
Quilimmune-M -- Antigenics
R 101933
R 125224 -- Sankyo
RA therapy -- Cardion
Rabies vaccine recombinant -- Aventis Pasteur, BioChem Vaccines, Kaketsuken Pharmaceuticals
RadioTheraCIM -- YM BioSciences
Ramot project No. 1315 -- Ramot
Ramot project No. K-734A -- Ramot
Ramot project No. K-734B -- Ramot
RANK -- Immunex
ranpirnase -- Alfacell
ranpirnase-anti-CD22 MAb -- Alfacell
RANTES inhibitor -- Milan
RAPID drug delivery systems -- ARIAD
rasburicase -- Sanofi
rBPI-21, topical -- XOMA
RC 529 -- Corixa
rCFTR -- Genzyme Transgenics
RD 62198
rDnase -- Genentech
RDP-58 -- SangStat

FIG. 1X

RecepTox-Fce -- Keryx
RecepTox-GnRH – Keryx, MTR Technologies
RecepTox-MBP – Keryx, MTR Technologies
recFSH -- Akzo Nobel, Organon
REGA 3G12
Regavirumab -- Teijin
relaxin -- Connetics Corp
Renal cancer vaccine -- Macropharm
repifermin -- Human Genome Sciences
Respiratory syncytial virus PFP-2 vaccine -- Wyeth-Lederle
Respiratory syncytial virus vaccine – GlaxoSmithKline, Pharmacia, Pierre Fabre
Respiratory syncytial virus vaccine inactivated
Respiratory syncytial virus-parainfluenza virus vaccine -- Aventis Pasteur, Pharmacia
Reteplase -- Boehringer Mannheim, Hoffman La-Roche
Retropep -- Retroscreen
RFB4 (dsFv) PE38
RFI 641 -- American Home Products
RFTS -- UAB Research Foundation
RG 12986 -- Aventis Pasteur
RG 83852 -- Aventis Pasteur
RG-1059 -- RepliGen
rGCR -- NIH
rGLP-1 -- Restoragen
rGRF -- Restoragen
rh Insulin – Eli Lilly
RHAMM targeting peptides -- Cangene
rHb1.1 – Baxter Intl.
rhCC10 -- Claragen
rhCG -- Serono
Rheumatoid arthritis gene therapy
Rheumatoid arthritis vaccine -- Veterans Affairs Medical Center
rhLH -- Serono
Ribozyme gene therapy -- Genset
Rickettsial vaccine recombinant
RIGScan CR -- Neoprobe
RIP-3 -- Rigel
RK-0202 -- RxKinetix
RLT peptide -- Esperion
rM/NEI -- IVAX
rmCRP -- Immtech
RN-1001 -- Renovo
RN-3 -- Renovo
RNAse conjugate -- Immunomedics
RO 631908 -- Roche
Rotavirus vaccine -- Merck
RP 431 -- DuPont Pharmaceuticals
RP-128 -- Resolution
RPE65 gene therapy –
RPR 110173 -- Aventis Pasteur
RPR 115135 -- Aventis Pasteur
RPR 116258A -- Aventis Pasteur
rPSGL-Ig -- American Home Products
r-SPC surfactant -- Byk Gulden
rV-HER-2/neu -- Therion Biologics
SA 1042 -- Sankyo
sacrosidase – Orphan Medical
Sant 7
Sargramostim -- Immunex
saruplase -- Gruenenthal
Satumomab -- Cytogen
SB 1 -- COR Therapeutics
SB 207448 -- GlaxoSmithKline
SB 208651 -- GlaxoSmithKline
SB 240683 -- GlaxoSmithKline
SB 249415 -- GlaxoSmithKline
SB 249417 -- GlaxoSmithKline
SB 6 -- COR Therapeutics
SB RA 31012 –
SC 56929 -- Pharmacia
SCA binding proteins – Curis, Enzon
scFv(14E1)-ETA Berlex Laboratories, Schering AG
ScFv(FRP5)-ETA –

FIG. 1Y

ScFv6C6-PE40 –
SCH 55700 -- Celltech
Schistosomiasis vaccine -- Glaxo Wellcome/Medeva, Brazil
SCPF -- Advanced Tissue Sciences
scuPA-suPAR complex -- Hadasit
SD-9427 -- Pharmacia
SDF-1 -- Ono
SDZ 215918 -- Novartis
SDZ 280125 -- Novartis
SDZ 89104 -- Novartis
SDZ ABL 364 -- Novartis
SDZ MMA 383 -- Novartis
serine protease inhibs -- Pharis
sermorelin acetate -- Serono
SERP-1 -- Viron
sertenef -- Dainippon
serum albumin, Recombinant human -- Aventis Behring
serum-derived factor -- Hadasit
Sevirumab -- Novartis
SGN 14 -- Seatle Genetics
SGN 15 -- Seatle Genetics
SGN 17/19 -- Seatle Genetics
SGN 30 -- Seatle Genetics
SGN-10 -- Seatle Genetics
SGN-11 -- Seatle Genetics
SH 306 -- DuPont Pharmaceuticals
Shanvac-B -- Shantha
Shigella flexneri vaccine – Avant, Acambis, Novavax
Shigella sonnei vaccine –
sICAM-1 -- Boehringer Ingelheim
Silteplase -- Genzyme
SIV vaccine -- Endocon, Institut Pasteur
SK 896 -- Sanwa Kagaku Kenkyusho
SK-827 -- Sanwa Kagaku Kenkyusho
Skeletex -- CellFactors
SKF 106160 -- GlaxoSmithKline
S-nitroso-AR545C –
SNTP -- Active Biotech
somatomedin-1 – GroPep, Mitsubishi-Tokyo, NIH
somatomedin-1 carrier protein -- Insmed
somatostatin -- Ferring
Somatotropin/
Human Growth Hormone -- Bio-Tech. General, Eli Lilly
somatropin -- Bio-Tech. General, Alkermes, ProLease, Aventis Behring, Biovector, Cangene, Dong-A, Eli Lilly, Emisphere, Enact, Genentech, Genzyme Transgenics, Grandis/InfiMed, CSL, InfiMed, MacroMed, Novartis, Novo Nordisk, Pharmacia Serono, TranXenoGen
somatropin derivative -- Schering AG
somatropin, AIR -- Eli Lilly
Somatropin, inhaled -- Eli Lilly/Alkermes
somatropin, Kabi -- Pharmacia
somatropin, Orasome -- Novo Nordisk
Sonermin -- Dainippon Pharmaceutical
SP(V5.2)C -- Supertek
SPf66
sphingomyelinase -- Genzyme
SR 29001 -- Sanofi
SR 41476 -- Sanofi
SR-29001 -- Sanofi
SS1(dsFV)-PE38 -- NeoPharm
ß2 microglobulin -- Avidex
ß2-microglobulin fusion proteins -- NIH
ß-amyloid peptides -- CeNeS
ß-defensin -- Pharis
Staphylococcus aureus infections -- Inhibitex/ZLB
Staphylococcus aureus vaccine conjugate -- Nabi
Staphylococcus therapy -- Tripep
Staphylokinase – Biovation, Prothera, Thrombogenetics
Streptococcal A vaccine -- M6 Pharmaceuticals, North American Vaccine
Streptococcal B vaccine -- Microscience

FIG. 1Z

Streptococcal B vaccine recombinant -- Biochem Vaccines
Streptococcus pyogenes vaccine
STRL-33 -- NIH
Subalin -- SRC VB VECTOR
SUIS -- United Biomedical
SUIS-LHRH -- United Biomedical
SUN-E3001 -- Suntory
super high affinity monoclonal antibodies -- YM BioSciences
Superoxide dismutase -- Chiron, Enzon, Ube Industries, Bio-Tech, Yeda
superoxide dismutase-2 -- OXIS
suppressin -- UAB Research Foundation
SY-161-P5 -- ThromboGenics
SY-162 -- ThromboGenics
Systemic lupus erythematosus vaccine -- MedClone/VivoRx
T cell receptor peptide vaccine
T4N5 liposomes -- AGI Dermatics
TACI, soluble -- ZymoGenetics
targeted apoptosis -- Antisoma
tasonermin -- Boehringer Ingelheim
TASP
TASP-V
Tat peptide analogues -- NIH
TBP I -- Yeda
TBP II
TBV25H -- NIH
Tc 99m ior cea1 -- Center of Molecular Immunology
Tc 99m P 748 -- Diatide
Tc 99m votumumab -- Intracell
Tc-99m rh-Annexin V -- Theseus Imaging
teceleukin -- Biogen
tenecteplase -- Genentech
Teriparatide -- Armour Pharmaceuticals, Asahi Kasei, Eli Lilly
terlipressin -- Ferring
testisin -- AMRAD
Tetrafibricin -- Roche
TFPI -- EntreMed
tgD-IL-2 -- Takeda
TGF-Alpha -- ZymoGenetics
TGF-ß -- Kolon
TGF-ß2 -- Insmed
TGF-ß3 -- OSI
Thalassaemia gene therapy -- Crucell
TheraCIM-h-R3 -- Center of Molecular Immunology, YM BioSciences
Theradigm-HBV -- Epimmune
Theradigm-HPV -- Epimmune
Theradigm-malaria -- Epimmune
Theradigm-melanoma -- Epimmune
TheraFab -- Antisoma
ThGRF 1-29 -- Theratechnologies
ThGRF 1-44 -- Theratechnologies
thrombomodulin -- Iowa, Novocastra
Thrombopoietin -- Dragon Pharmaceuticals, Genentech
thrombopoietin, Pliva -- Receptron
Thrombospondin 2 --
thrombostatin -- Thromgen
thymalfasin -- SciClone
thymocartin -- Gedeon Richter
thymosin Alpha1 -- NIH
thyroid stimulating hormone -- Genzyme
tICAM-1 -- Bayer
Tick anticoagulant peptide -- Merck
TIF -- Xoma
Tifacogin -- Chiron, NIS, Pharmacia
Tissue factor -- Genentech
Tissue factor pathway inhibitor
TJN-135 -- Tsumura
TM 27 -- Avant
TM 29 -- Avant
TMC-151 -- Tanabe Seiyaku
TNF tumour necrosis factor -- Asahi Kasei
TNF Alpha -- CytImmune
TNF antibody -- Johnson & Johnson
TNF binding protein -- Amgen
TNF degradation product -- Oncotech

FIG. 1AA

TNF receptor -- Immunex
TNF receptor 1, soluble -- Amgen
TNF Tumour necrosis factor-alpha -- Asahi Kasei, Genetech, Mochida
TNF-Alpha inhibitor -- Tripep
TNFR:Fc gene therapy -- Targeted Genetics
TNF-SAM2
ToleriMab -- Innogenetics
Toxoplasma gondii vaccine -- GlaxoSmithKline
TP 9201 -- Telios
TP10 -- Avant
TP20 -- Avant
tPA -- Centocor
trafermin -- Scios
TRAIL/Apo2L -- Immunex
transferrin-binding proteins -- CAMR
Transforming growth factor-beta-1 -- Genentech
transport protein -- Genesis
TRH -- Ferring
Triabin -- Schering AG
Triconal
Triflavin
troponin I -- Boston Life Sciences
TRP-2^ -- NIH
trypsin inhibitor -- Mochida
TSP-1 gene therapy --
TT-232
TTS-CD2 -- Active Biotech
Tuberculosis vaccine -- Aventis Pasteur, Genesis
Tumor Targeted Superantigens -- Active Biotech -- Pharmacia
tumour vaccines -- PhotoCure
tumour-activated prodrug antibody conjugates -- Millennium/ImmunoGen
tumstatin -- ILEX
Tuvirumab -- Novartis
TV-4710 -- Teva
TWEAK receptor -- Immunex
TXU-PAP
TY-10721 -- TOA Eiyo
Type I diabetes vaccine -- Research Corp
Typhoid vaccine CVD 908
U 143677 -- Pharmacia
U 81749 -- Pharmacia
UA 1248 -- Arizona
UGIF -- Sheffield
UIC 2
UK 101
UK-279276 -- Corvas Intl.
urodilatin -- Pharis
urofollitrophin -- Serono
uteroferrin-- Pepgen
V 20 -- GLYCODesign
V2 vasopressin receptor gene therapy
vaccines -- Active Biotech
Varicella zoster glycoprotein vaccine -- Research Corporation Technologies
Varicella zoster virus vaccine live -- Cantab Pharmaceuticals
Vascular endothelial growth factor -- Genentech, University of California
Vascular endothelial growth factors -- R&D Systems
vascular targeting agents -- Peregrine
vasopermeation enhancement agents -- Peregrine
vasostatin -- NIH
VCL -- Bio-Tech. General
VEGF -- Genentech, Scios
VEGF inhibitor -- Chugai
VEGF-2 -- Human Genome Sciences
VEGF-Trap -- Regeneron
viscumin, recombinant -- Madaus
Vitaxin
Vitrase -- ISTA Pharmaceuticals
West Nile virus vaccine -- Bavarian Nordic
WP 652
WT1 vaccine -- Corixa
WX-293 -- Wilex BioTech.

FIG. 1BB

WX-360 -- Wilex BioTech.
WX-UK1 -- Wilex BioTech.
XMP-500 -- XOMA
XomaZyme-791 -- XOMA
XTL 001 -- XTL Biopharmaceuticals
XTL 002 -- XTL Biopharmaceuticals
yeast delivery system -- GlobeImmune
Yersinia pestis vaccine
YIGSR-Stealth -- Johnson & Johnson
Yissum Project No. D-0460 -- Yissum
YM 207 -- Yamanouchi
YM 337 -- Protein Design Labs
Yttrium-90 labelled biotin
Yttrium-90-labeled anti-CEA MAb T84.66 –
ZD 0490 – AstraZeneca
ziconotide -- Elan
ZK 157138 -- Berlex Laboratories
Zolimomab aritox
Zorcell -- Immune Response
ZRXL peptides -- Novartis

FIG. 1CC

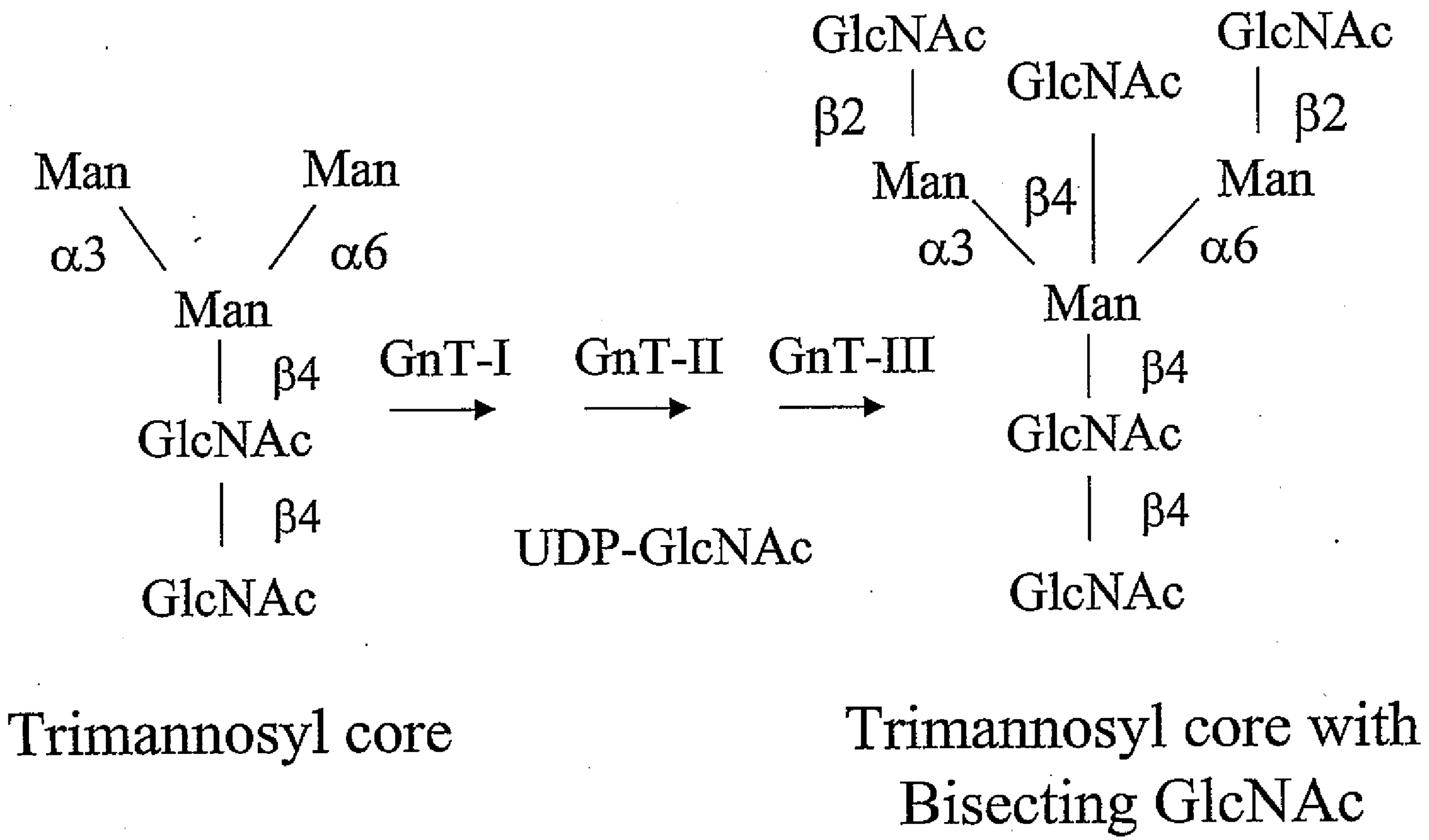

Man
Man
α3
α6
Man
β4
GlcNAc
β4
GlcNAc
GnT-I
GnT-II
GnT-III
UDP-GlcNAc
GlcNAc
GlcNAc
GlcNAc
β2
β2
Man
β4
Man
α3
α6
Man
β4
GlcNAc
β4
GlcNAc
Trimannosyl core
Trimannosyl core with Bisecting GlcNAc

FIG. 2

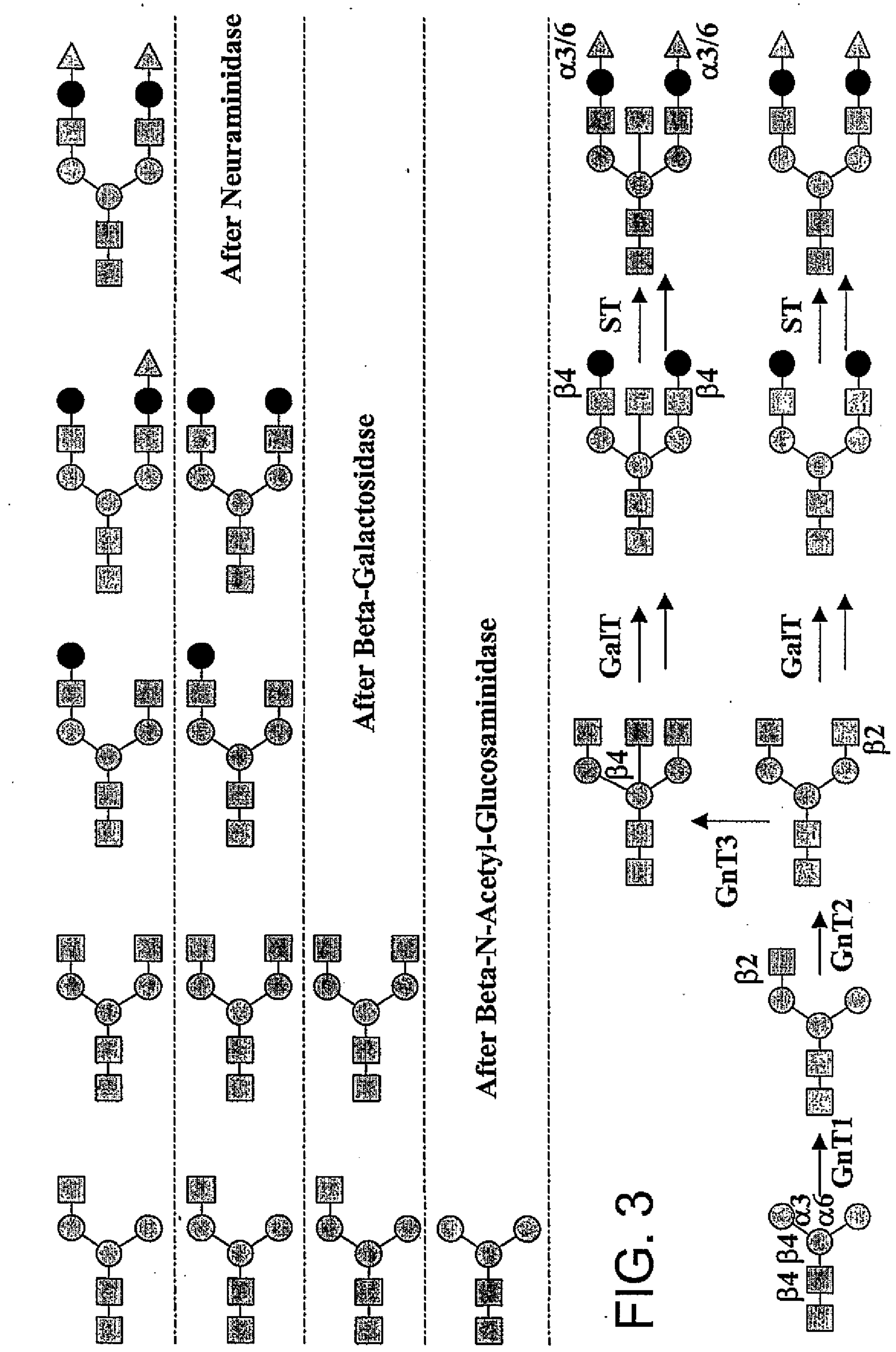

After Neuraminidase
After Beta-Galactosidase
After Beta-N-Acetyl-Glucosaminidase
β4 β4
α3
α6
GnT1
β2
GnT2
GnT3
β4
β2
GalT
GalT
β4
β4
ST
ST
α3/6
α3/6

FIG. 3

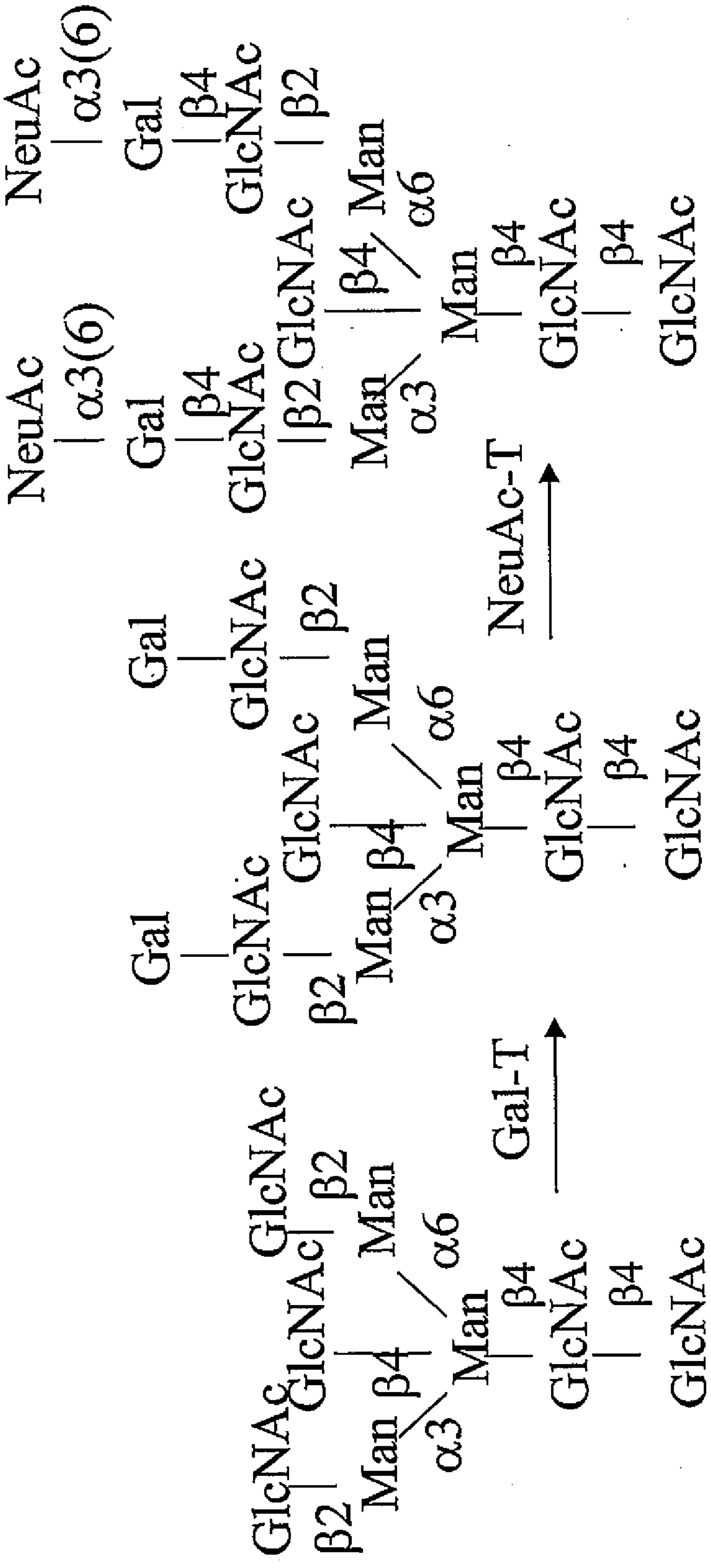

GlcNAc
β2
Man
α3
GlcNAc
GlcNAc
β4
Man
GlcNAc
β2
Man
α6
β4
GlcNAc
β4
GlcNAc
Gal-T
Gal
GlcNAc
β2
Man
α3
Gal
GlcNAc
GlcNAc
β4
Man
GlcNAc
β2
Man
α6
β4
GlcNAc
β4
GlcNAc
NeuAc-T
NeuAc
α3(6)
Gal
β4
GlcNAc
β2
Man
α3
NeuAc
α3(6)
Gal
β4
GlcNAc
β2
Man
α6
GlcNAc
β4
Man
β4
GlcNAc
β4
GlcNAc

FIG. 4

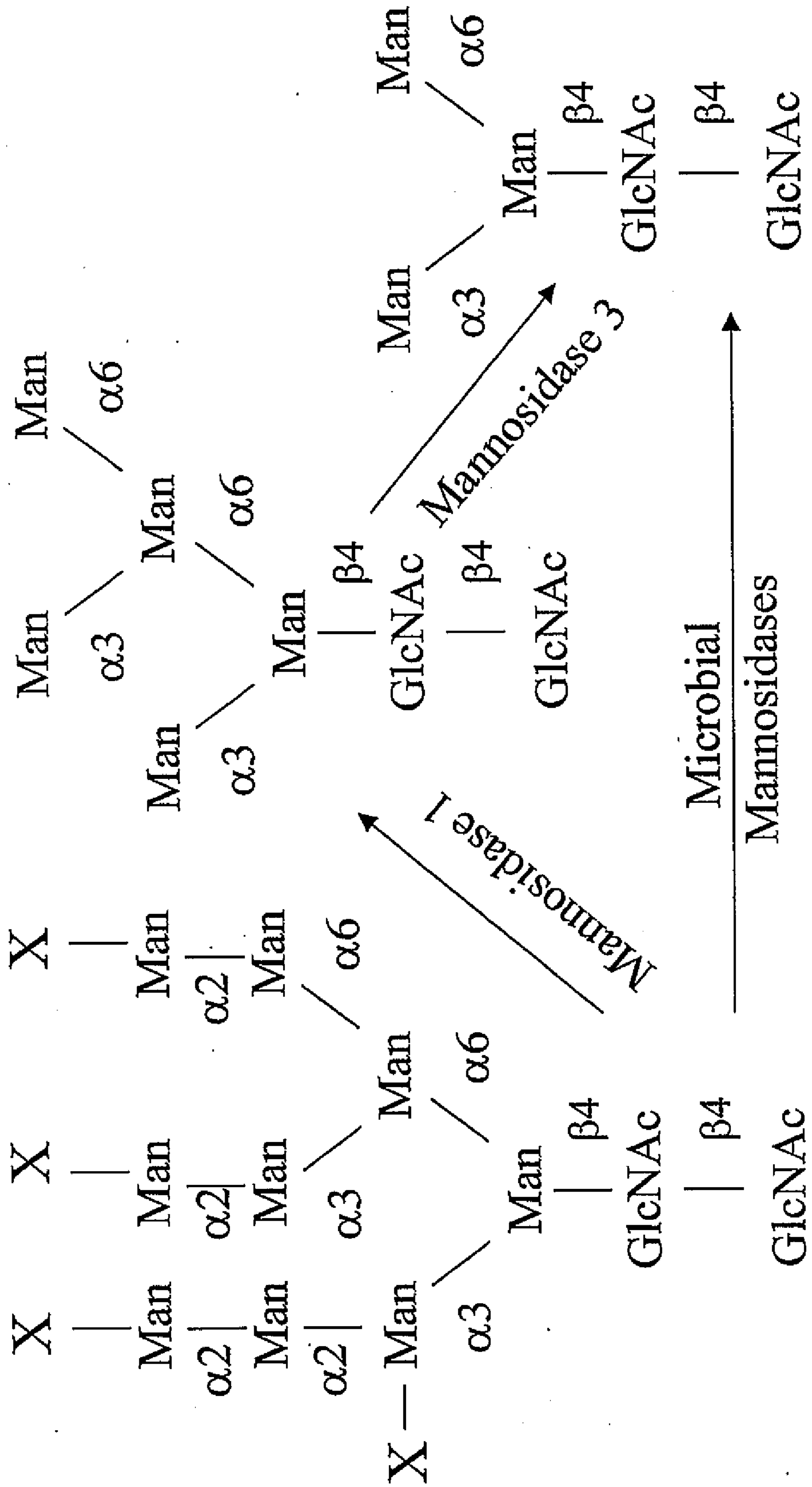

X
X
X
X
Man
α2
α3
α6
β4
GlcNAc
Mannosidase 1
Mannosidase 3
Microbial
Mannosidases

FIG. 5

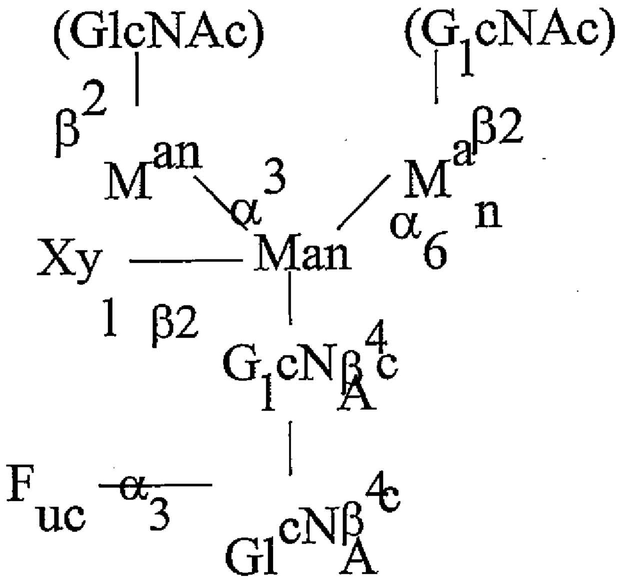

(GlcNAc)
(G1cNAc)
β2
Man
α3
Maβ2n
α6
Xy
1 β2
Man
G1cNβ4cA
Fuc
α3
GlcNβ4cA

FIG. 6

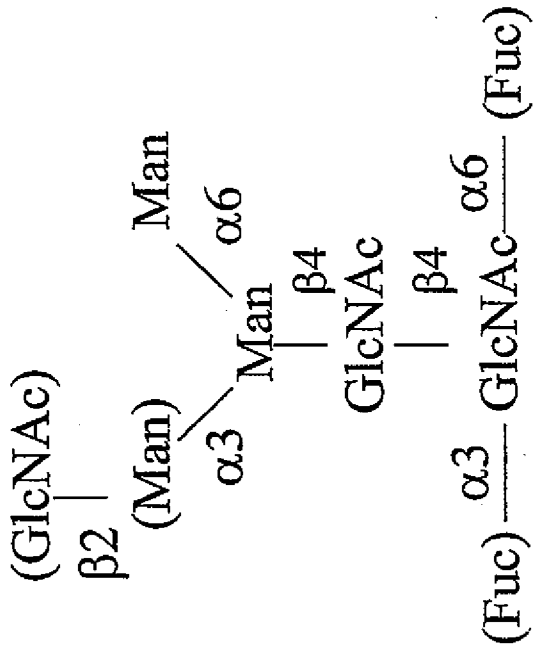


FIG. 7

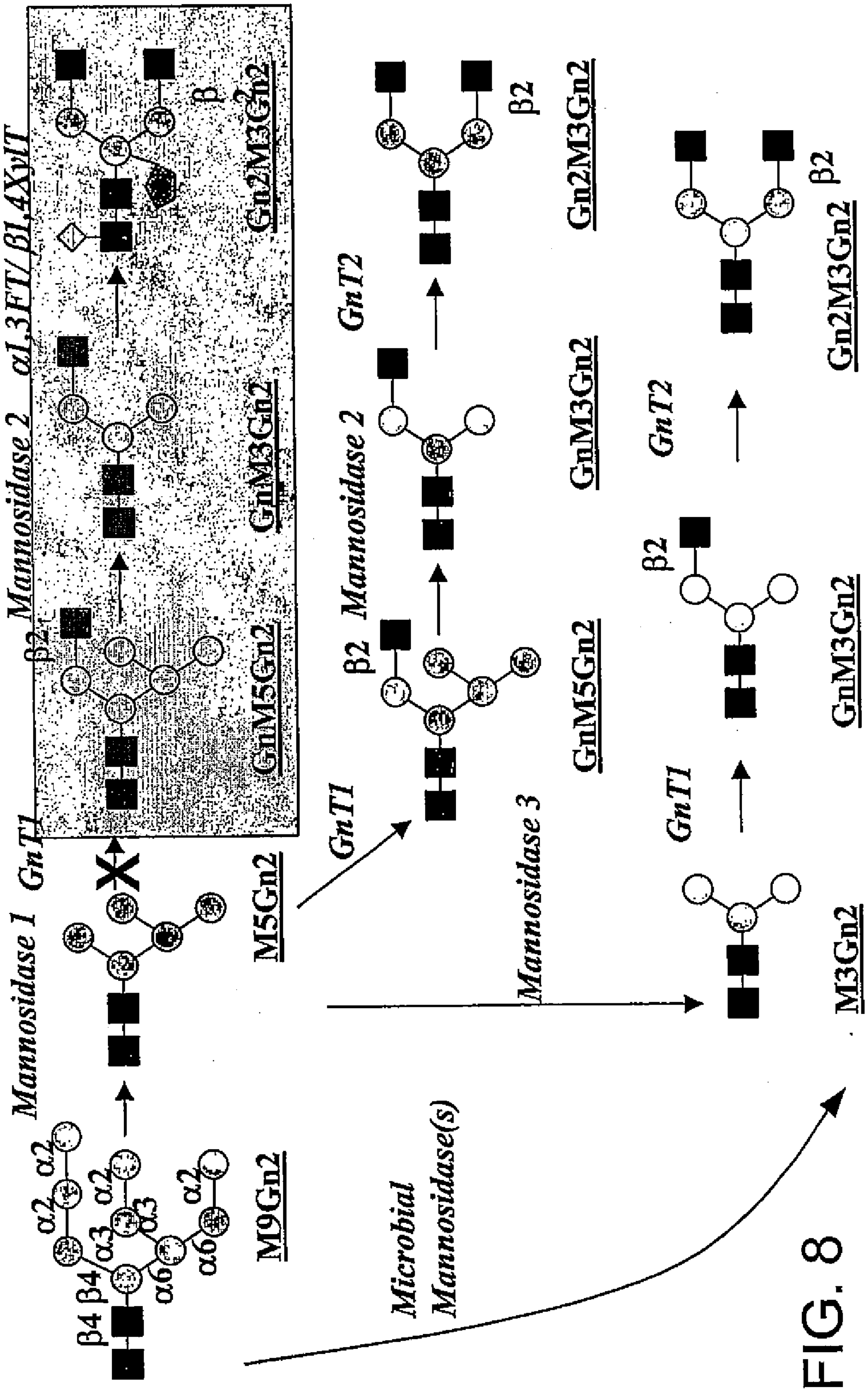

Mannosidase 1
GnT1
Mannosidase 2
α1,3FT/β1,4XylT
β4
β4
α2
α2
α3
α2
α3
α6
α6
α2
β2
β
2
M9Gn2
M5Gn2
GnM5Gn2
GnM3Gn2
Gn2M3Gn2
GnT1
β2
Mannosidase 2
GnT2
β2
GnM5Gn2
GnM3Gn2
Gn2M3Gn2
Mannosidase 3
GnT1
β2
GnT2
β2
M3Gn2
GnM3Gn2
Gn2M3Gn2
Microbial
Mannosidase(s)

FIG. 8

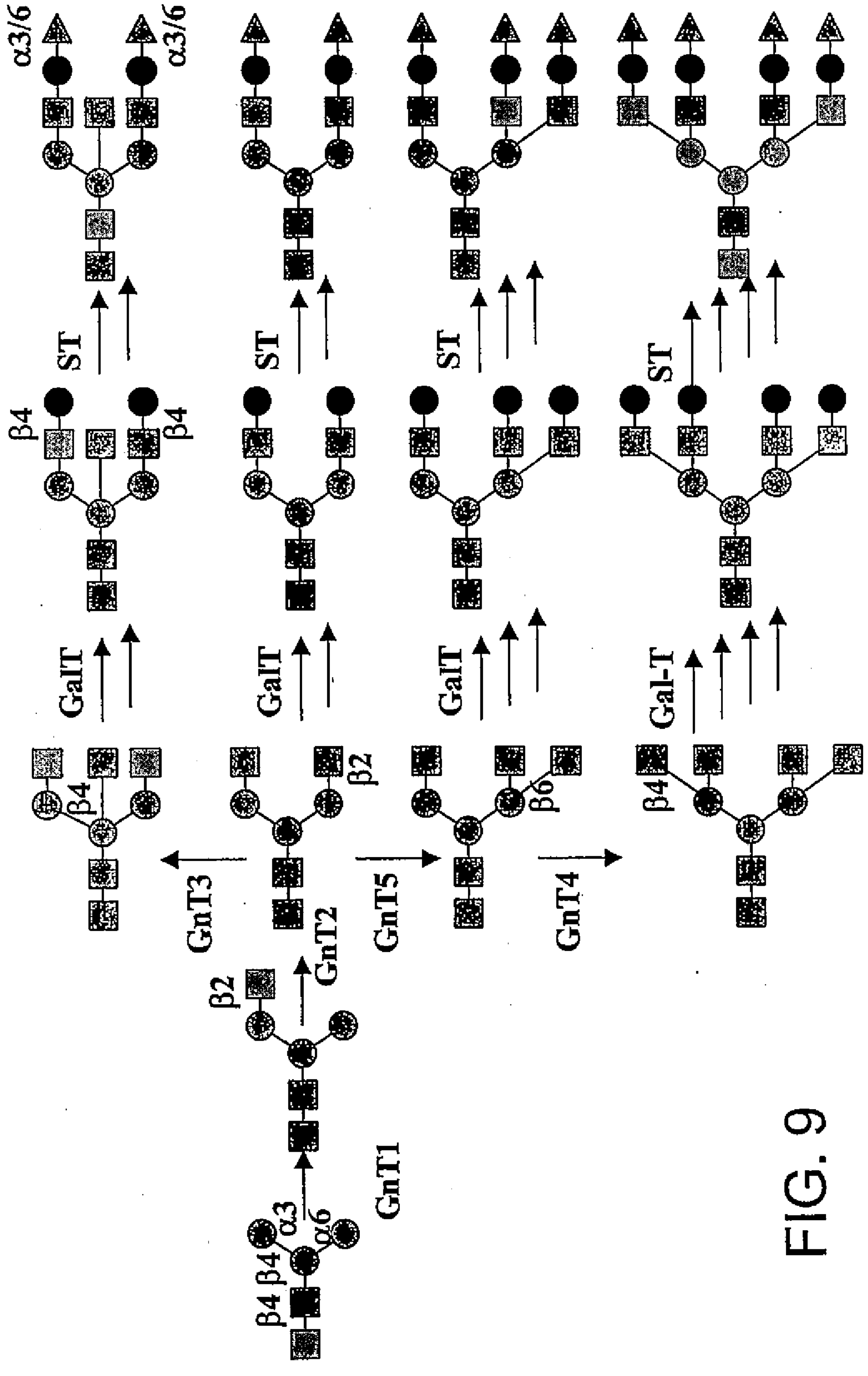

β4
β4
α3
α6
GnT1
β2
GnT2
GnT3
β4
GnT5
β2
β6
GnT4
β4
GalT
GalT
GalT
Gal-T
β4
β4
ST
ST
ST
ST
α3/6
α3/6

FIG. 9

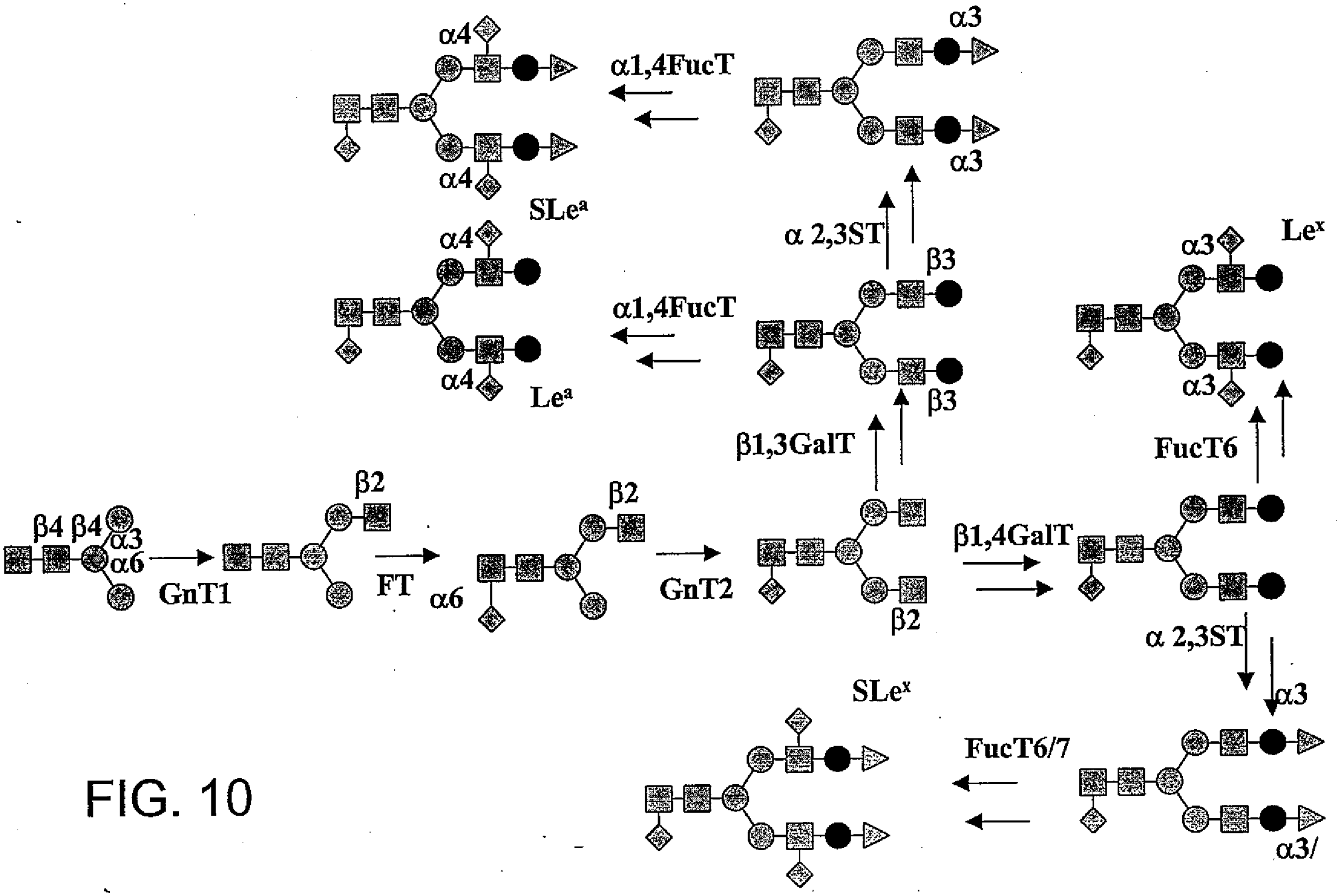

β4 β4
α3
α6
GnT1
β2
FT
α6
β2
GnT2
β2
β1,3GalT
β3
β3
α 2,3ST
α3
α3
α1,4FucT
α4
α4
SLeª
α1,4FucT
α4
α4
Leª
β1,4GalT
FucT6
α3
α3
Leˣ
α 2,3ST
α3
α3/
FucT6/7
SLeˣ

FIG. 10

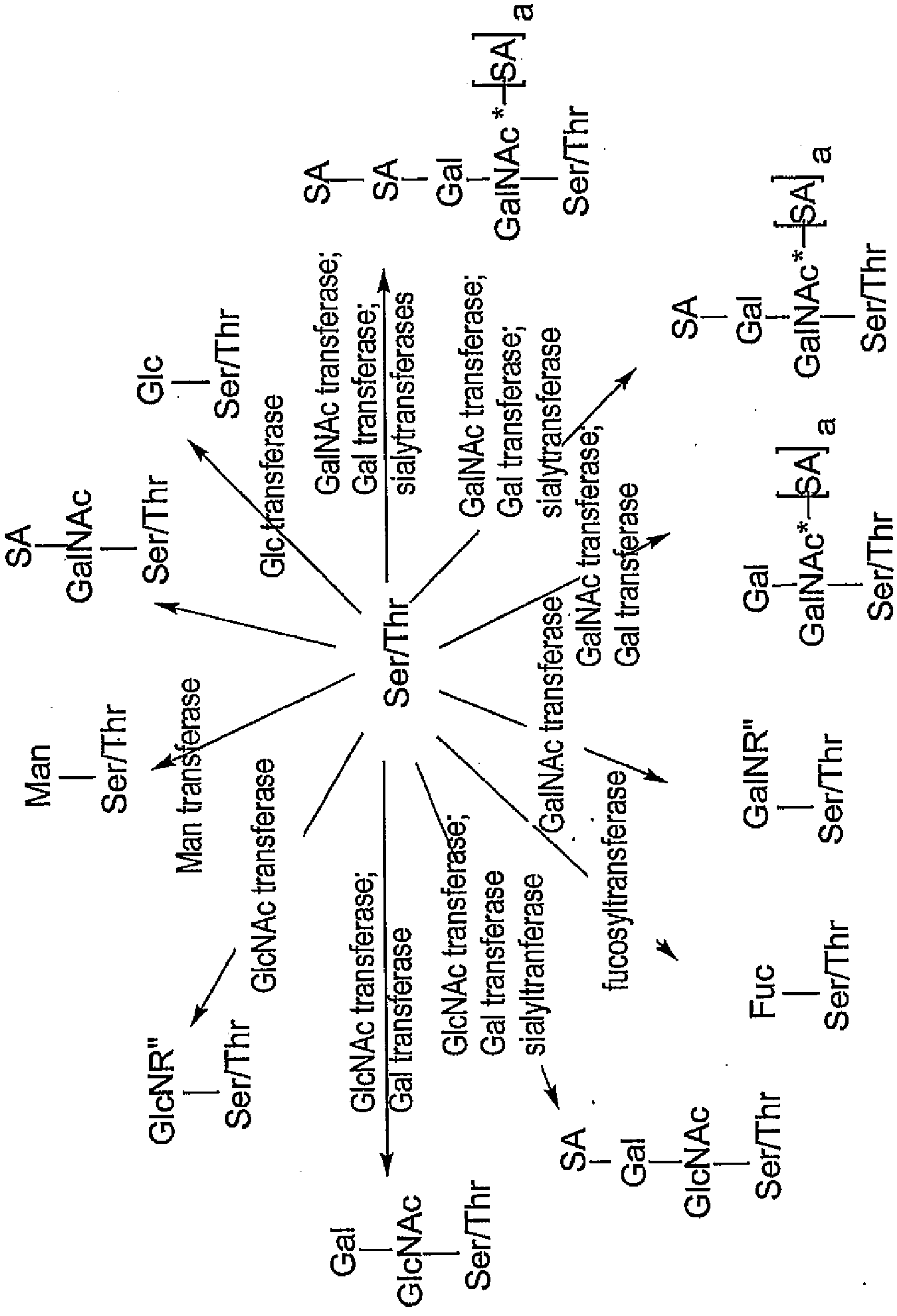

Ser/Thr
SA
GalNAc
Ser/Thr
Man
Ser/Thr
Man transferase
Glc
Ser/Thr
Glc transferase
GalNAc transferase; Gal transferase; sialytransferases
SA
SA
Gal
GalNAc *
[SA] a
Ser/Thr
GalNAc transferase; Gal transferase; sialytransferase
SA
Gal
GalNAc*
[SA] a
Ser/Thr
GalNAc transferase
Gal transferase
Gal
GalNAc*
[SA] a
Ser/Thr
GalNAc transferase
GalNR"
Ser/Thr
fucosyltransferase
Fuc
Ser/Thr
GlcNAc transferase; Gal transferase sialyltranferase
SA
Gal
GlcNAc
Ser/Thr
GlcNAc transferase; Gal transferase
Gal
GlcNAc
Ser/Thr
GlcNAc transferase
GlcNR"
Ser/Thr

FIG. 11

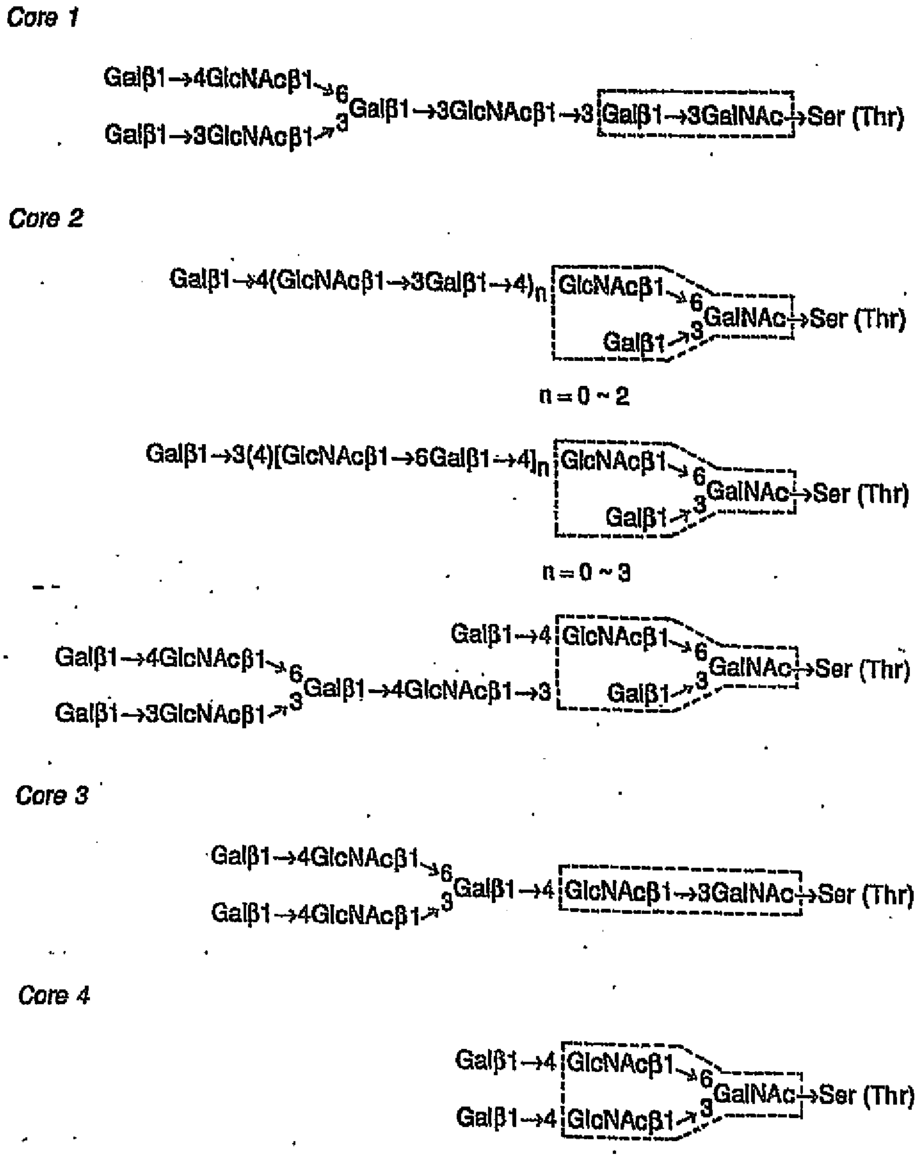
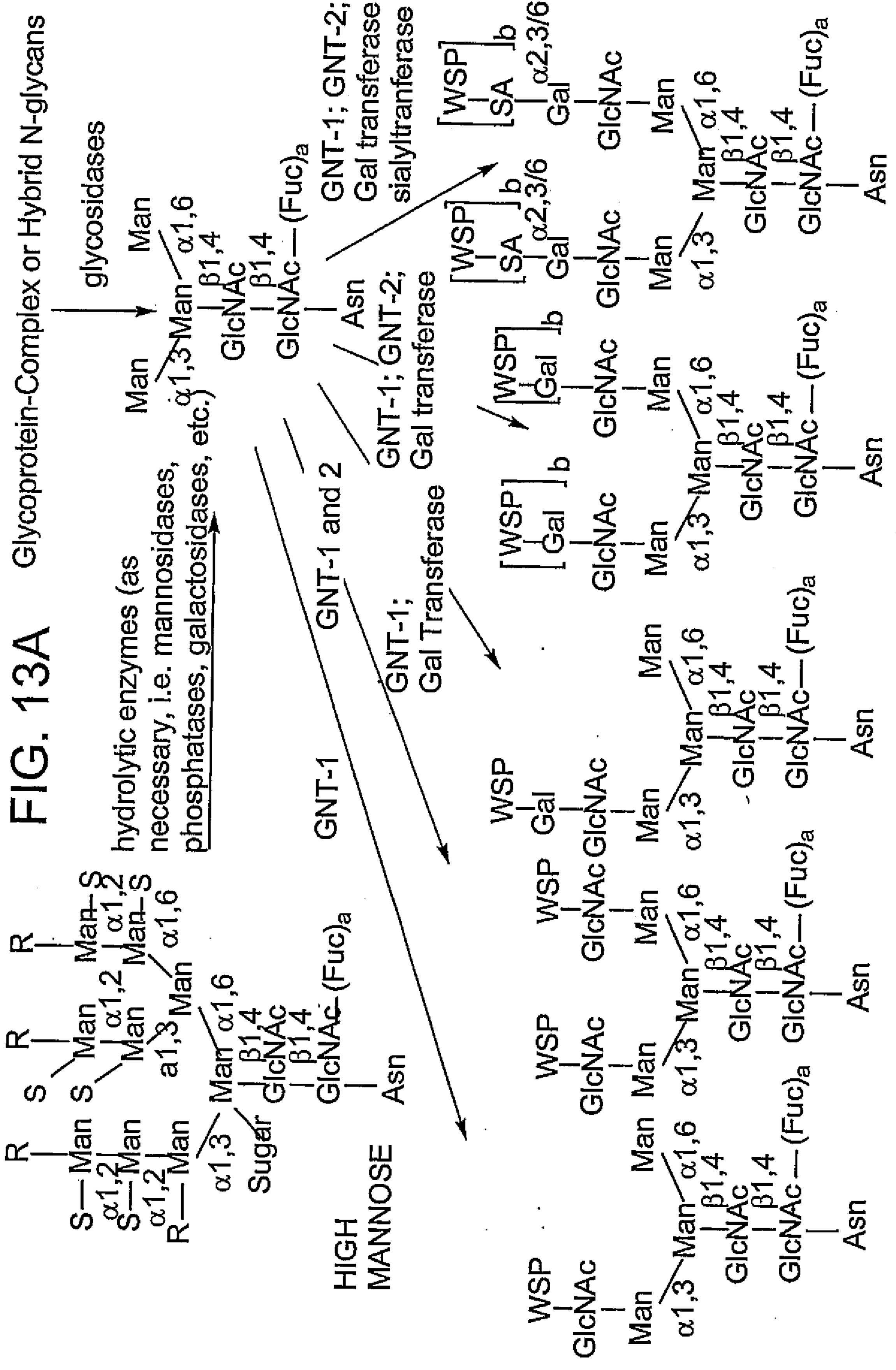

Core 1
Galβ1→4GlcNAcβ1→6
Galβ1→3GlcNAcβ1→3
Galβ1→3GlcNAcβ1→3
Galβ1→3GalNAc→Ser (Thr)
Core 2
Galβ1→4(GlcNAcβ1→3Galβ1→4)n
GlcNAcβ1→6
Galβ1→3
GalNAc→Ser (Thr)
n=0~2
Galβ1→3(4)[GlcNAcβ1→6Galβ1→4]n
GlcNAcβ1→6
Galβ1→3
GalNAc→Ser (Thr)
n=0~3
Galβ1→4
GlcNAcβ1→6
Galβ1→4GlcNAcβ1→6
Galβ1→3GlcNAcβ1→3
Galβ1→4GlcNAcβ1→3
Galβ1→3
GalNAc→Ser (Thr)
Core 3
Galβ1→4GlcNAcβ1→6
Galβ1→4GlcNAcβ1→3
Galβ1→4
GlcNAcβ1→3GalNAc→Ser (Thr)
Core 4
Galβ1→4
GlcNAcβ1→6
Galβ1→4
GlcNAcβ1→3
GalNAc→Ser (Thr)

FIG. 12

FIG. 13A


Glycoprotein-Complex or Hybrid N-glycans
glycosidases
hydrolytic enzymes (as necessary, i.e. mannosidases, phosphatases, galactosidases, etc.)
HIGH MANNOSE
R S R R S S
Man α1,2 Man α1,2 Man α1,3 Man α1,6 Man α1,2 Man α1,6
Sugar
Man α1,3 Man α1,6
GlcNAc β1,4 GlcNAc β1,4
(Fuc)a
Asn
GNT-1
GNT-1 and 2
GNT-1; Gal Transferase
GNT-1; GNT-2; Gal transferase
GNT-1; GNT-2; Gal transferase; sialyltranferase
WSP
GlcNAc
Gal
[WSP]
[Gal]b
[SA]b
α2,3/6

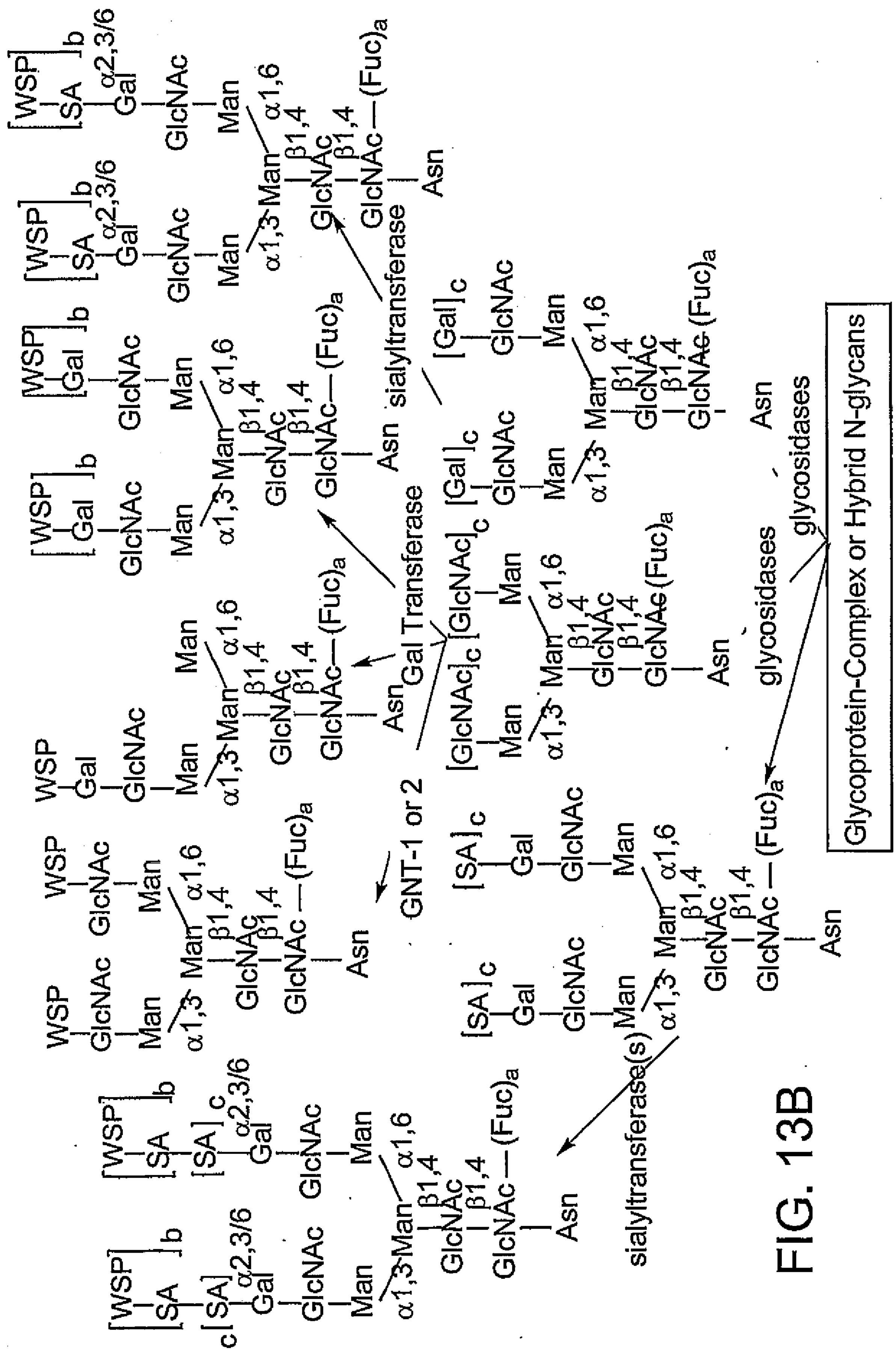

Glycoprotein-Complex or Hybrid N-glycans
glycosidases
glycosidases
glycosidases
GNT-1 or 2
Gal Transferase
sialyltransferase
sialyltransferase(s)
WSP
SA
Gal
GlcNAc
Man
α1,3
α1,6
β1,4
α2,3/6
Asn
(Fuc)a
[GlcNAc]c
[Gal]c
[SA]c
b
c

FIG. 13B

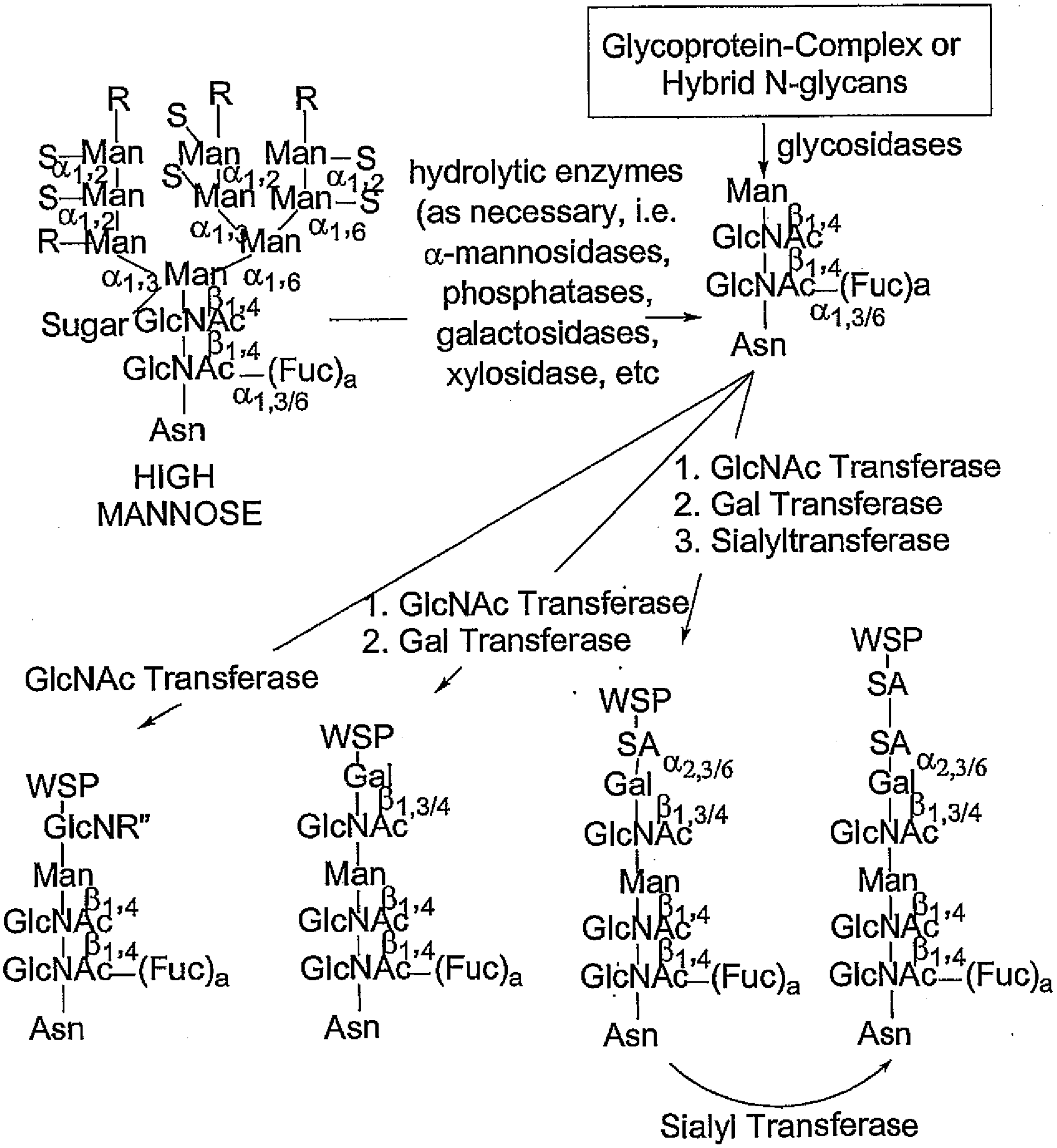

R
S
R
R
S—Man
Man
Man—S
α1,2
α1,2
α1,2
S—Man
S
Man
Man—S
α1,2
α1,3
Man
α1,6
R—Man
α1,3
Man
α1,6
β1,4
Sugar GlcNAc
β1,4
GlcNAc—(Fuc)a
α1,3/6
Asn
HIGH MANNOSE
hydrolytic enzymes (as necessary, i.e. α-mannosidases, phosphatases, galactosidases, xylosidase, etc
Glycoprotein-Complex or Hybrid N-glycans
glycosidases
Man
β1,4
GlcNAc
β1,4
GlcNAc—(Fuc)a
α1,3/6
Asn
1. GlcNAc Transferase
2. Gal Transferase
3. Sialyltransferase
1. GlcNAc Transferase
2. Gal Transferase
GlcNAc Transferase
WSP
GlcNR"
Man
β1,4
GlcNAc
β1,4
GlcNAc—(Fuc)a
Asn
WSP
Gal
β1,3/4
GlcNAc
Man
β1,4
GlcNAc
β1,4
GlcNAc—(Fuc)a
Asn
WSP
SA
α2,3/6
Gal
β1,3/4
GlcNAc
Man
β1,4
GlcNAc
β1,4
GlcNAc—(Fuc)a
Asn
WSP
SA
SA
α2,3/6
Gal
β1,3/4
GlcNAc
Man
β1,4
GlcNAc
β1,4
GlcNAc—(Fuc)a
Asn
Sialyl Transferase

FIG. 14

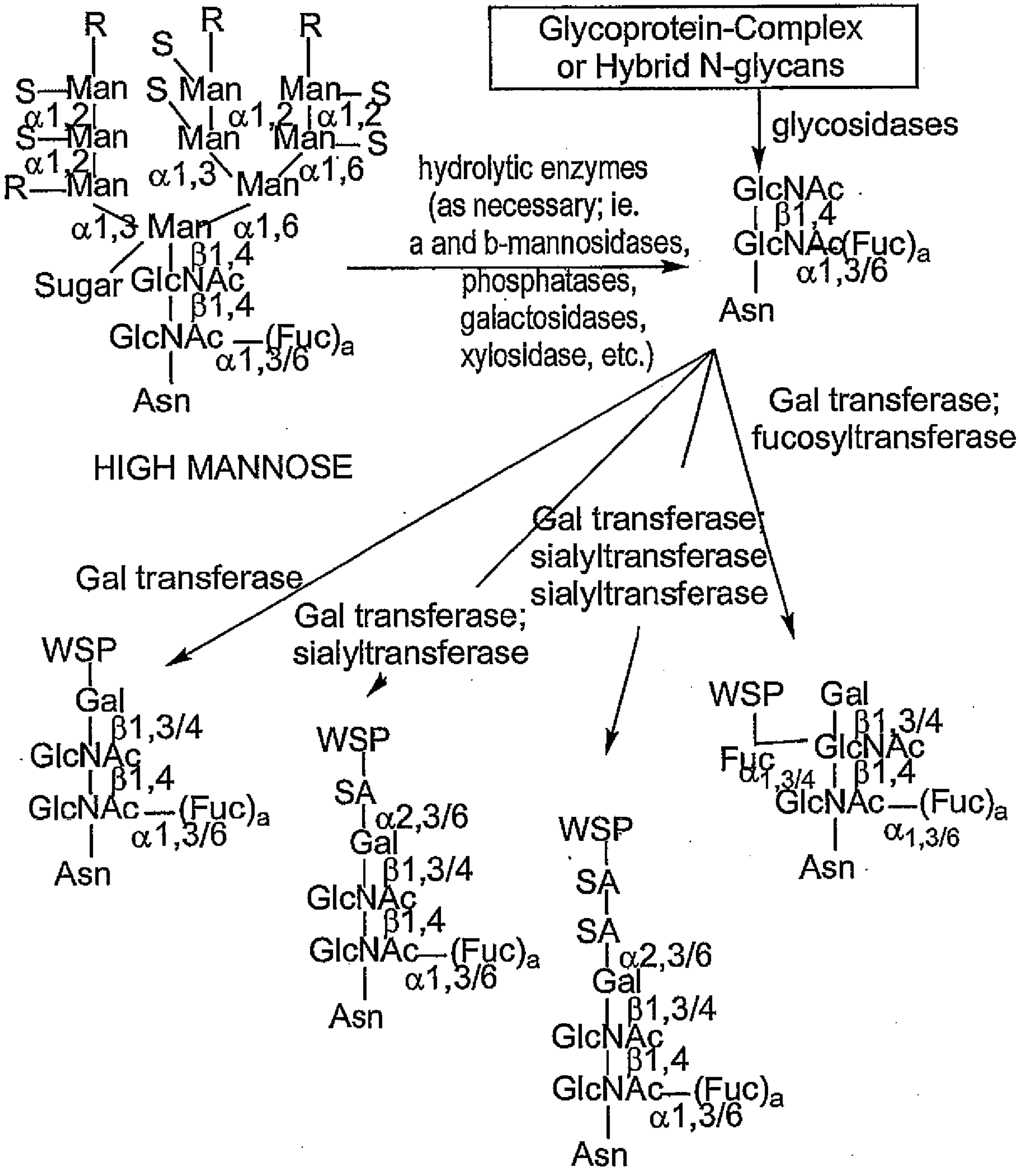

R
S
R
R
S—Man
S Man
Man—S
α1,2
α1,2
α1,2
S—Man
Man
Man—S
α1,2
R—Man
α1,3
Man
α1,6
α1,3 Man α1,6
β1,4
Sugar GlcNAc
β1,4
GlcNAc —(Fuc)a
α1,3/6
Asn
HIGH MANNOSE
Glycoprotein-Complex or Hybrid N-glycans
glycosidases
hydrolytic enzymes (as necessary; ie. a and b-mannosidases, phosphatases, galactosidases, xylosidase, etc.)
GlcNAc
β1,4
GlcNAc(Fuc)a
α1,3/6
Asn
Gal transferase; fucosyltransferase
Gal transferase
Gal transferase; sialyltransferase
Gal transferase; sialyltransferase sialyltransferase
WSP
Gal
β1,3/4
GlcNAc
β1,4
GlcNAc —(Fuc)a
α1,3/6
Asn
WSP
SA
α2,3/6
Gal
β1,3/4
GlcNAc
β1,4
GlcNAc—(Fuc)a
α1,3/6
Asn
WSP
SA
SA
α2,3/6
Gal
β1,3/4
GlcNAc
β1,4
GlcNAc—(Fuc)a
α1,3/6
Asn
WSP
Gal
β1,3/4
Fuc
GlcNAc
α1,3/4
β1,4
GlcNAc—(Fuc)a
α1,3/6
Asn

FIG. 15

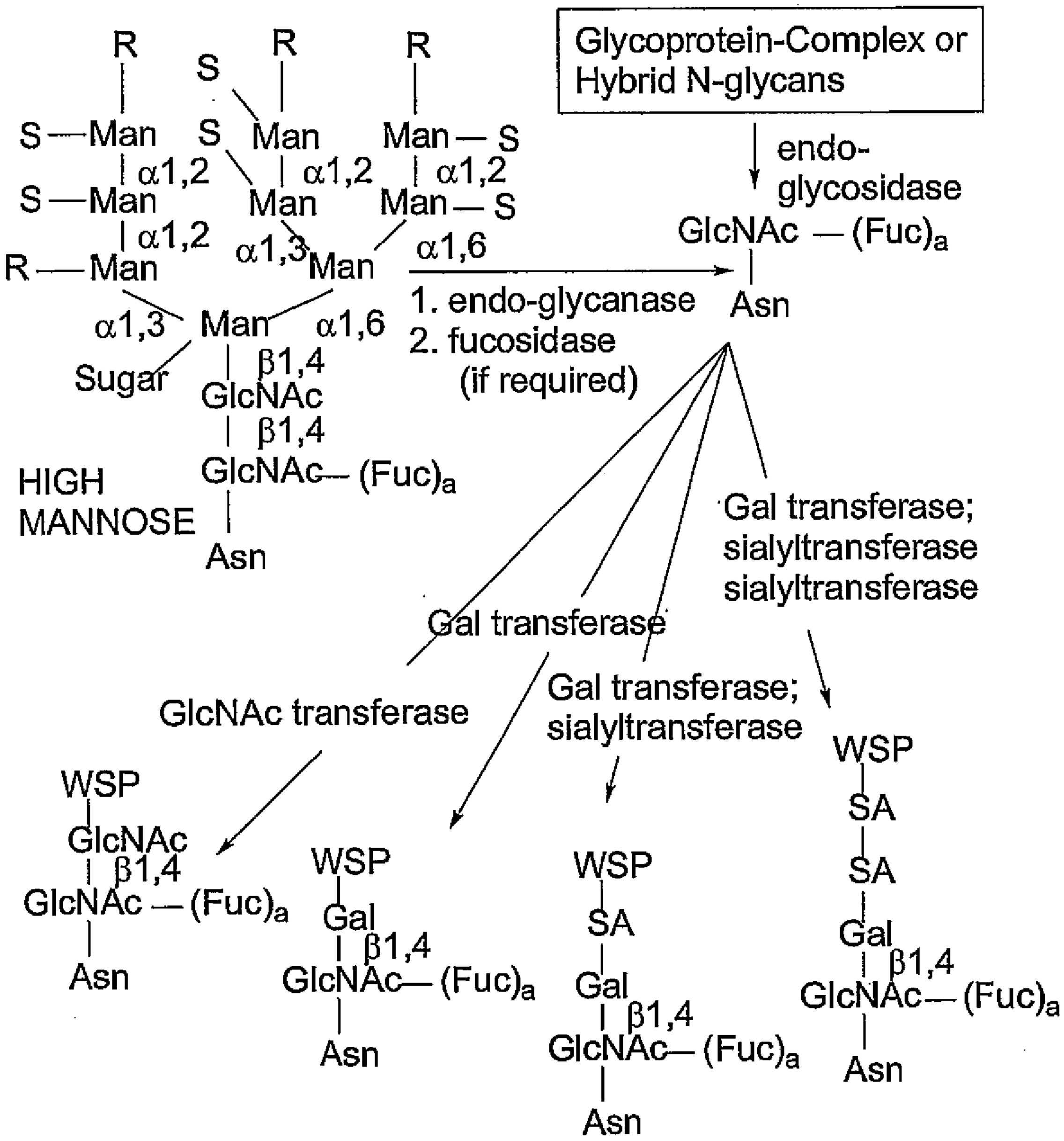

Glycoprotein-Complex or Hybrid N-glycans
endo-glycosidase
GlcNAc — (Fuc)a
Asn
R
S
Man
α1,2
α1,3
α1,6
Sugar
β1,4
GlcNAc
GlcNAc— (Fuc)a
HIGH MANNOSE
Asn
1. endo-glycanase
2. fucosidase (if required)
GlcNAc transferase
Gal transferase
Gal transferase; sialyltransferase
Gal transferase; sialyltransferase sialyltransferase
WSP
GlcNAc
Gal
SA

FIG. 16

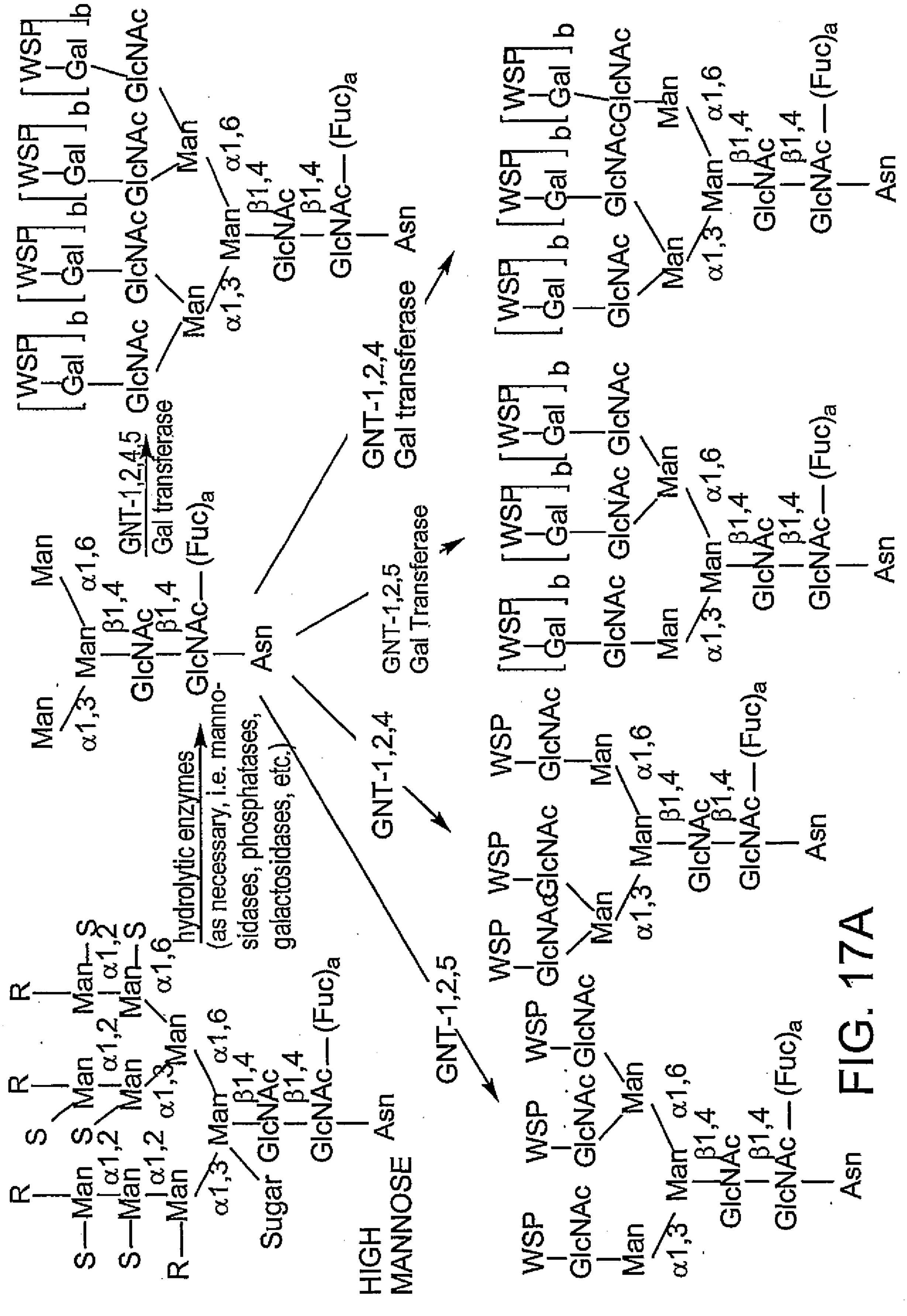

HIGH MANNOSE
R
S
Man
α1,2
α1,3
α1,6
Sugar
GlcNAc
β1,4
(Fuc)a
Asn
hydrolytic enzymes
(as necessary, i.e. mannosidases, phosphatases, galactosidases, etc.)
GNT-1,2,4,5
Gal transferase
GNT-1,2,5
GNT-1,2,4
GNT-1,2,5
Gal Transferase
GNT-1,2,4
Gal transferase
WSP
Gal
b

FIG. 17A

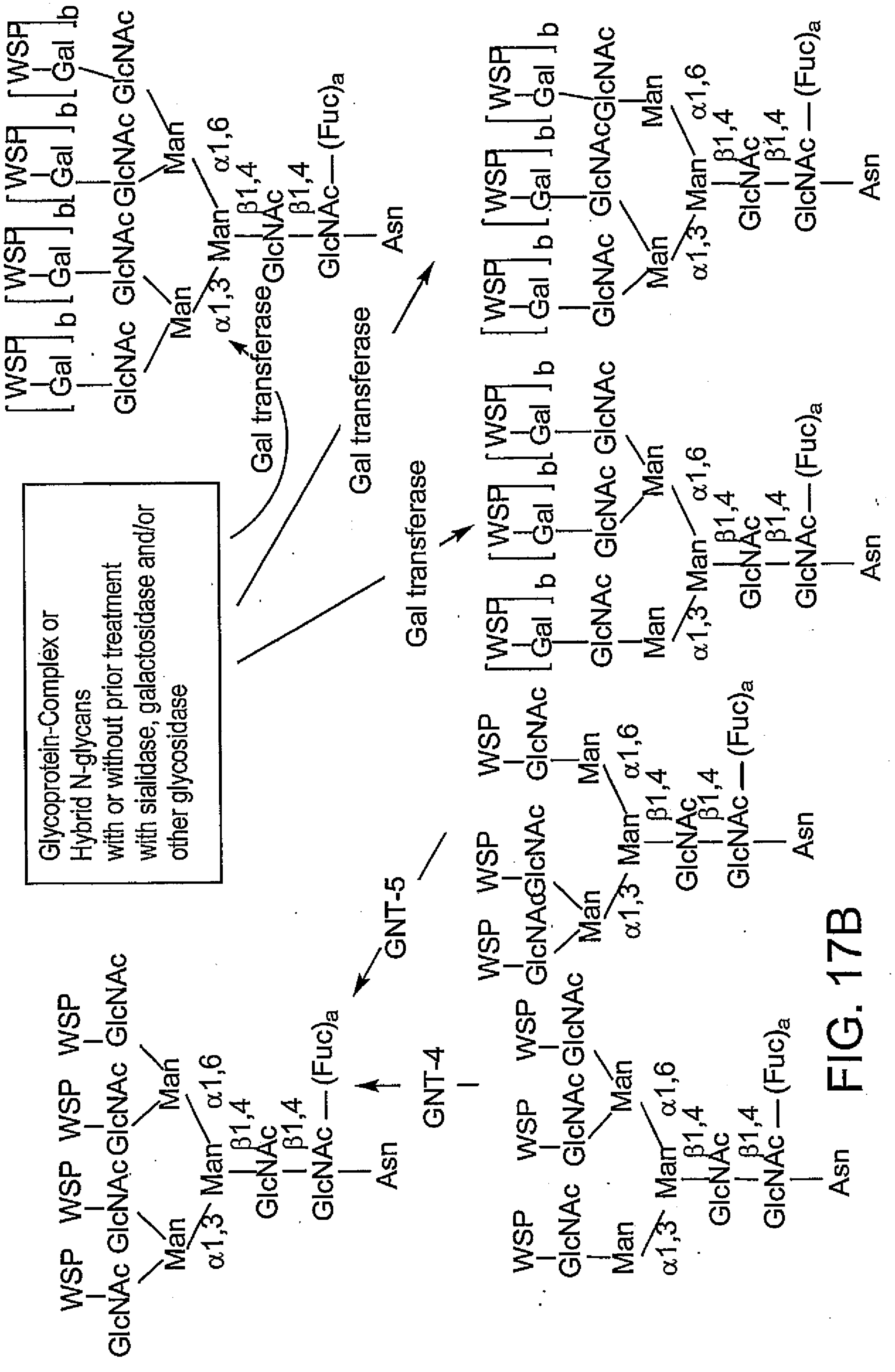

Glycoprotein-Complex or Hybrid N-glycans with or without prior treatment with sialidase, galactosidase and/or other glycosidase
Gal transferase
Gal transferase
Gal transferase
GNT-4
GNT-5
WSP
Gal
GlcNAc
Man
α1,3
α1,6
β1,4
Asn
(Fuc)a
b

FIG. 17B

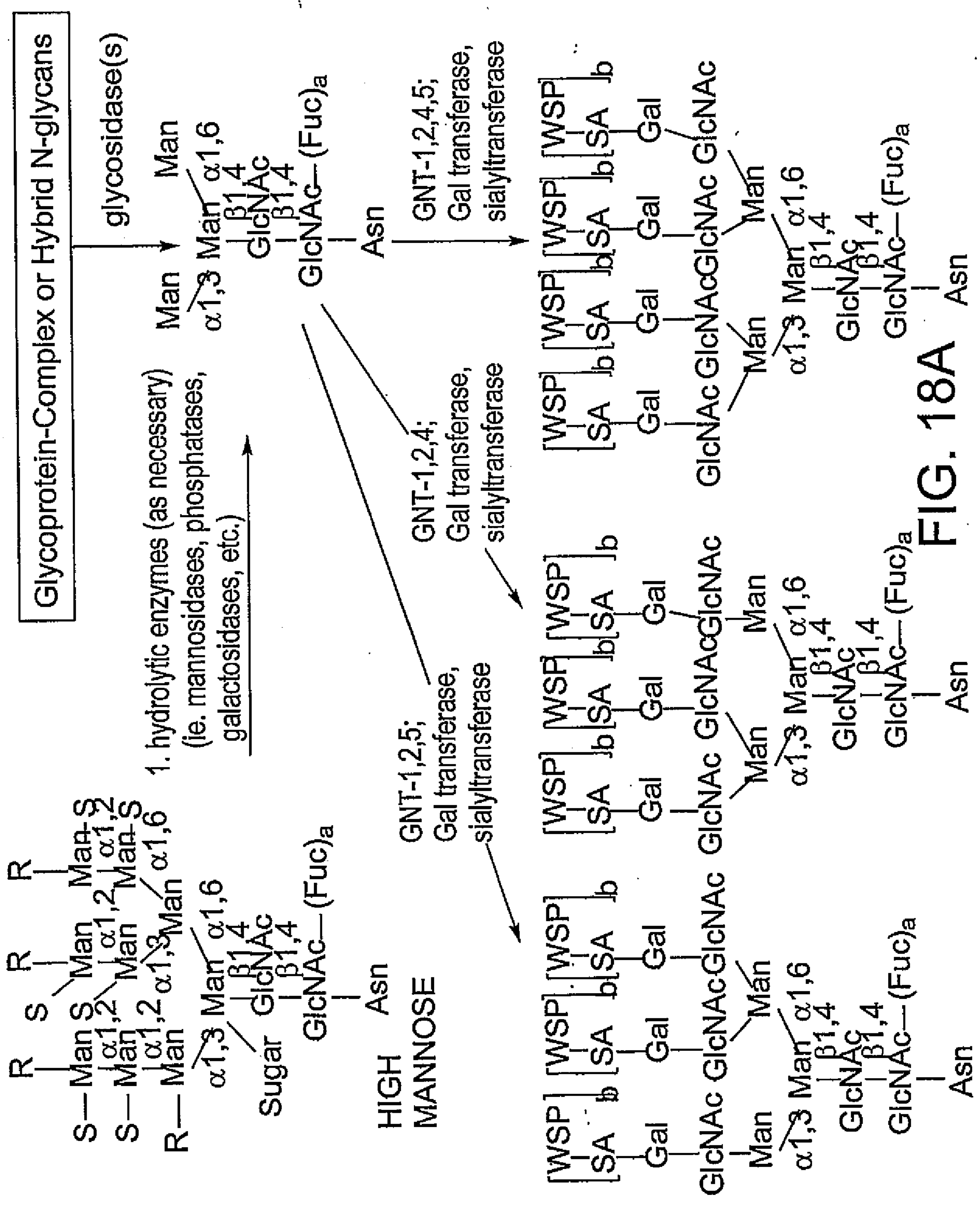

Glycoprotein-Complex or Hybrid N-glycans
glycosidase(s)
1. hydrolytic enzymes (as necessary) (ie. mannosidases, phosphatases, galactosidases, etc.)
HIGH MANNOSE
R
S
Man
α1,2
α1,3
α1,6
β1,4
GlcNAc
(Fuc)a
Asn
Sugar
GNT-1,2,5; Gal transferase, sialyltransferase
GNT-1,2,4; Gal transferase, sialyltransferase
GNT-1,2,4,5; Gal transferase, sialyltransferase
WSP
SA
Gal
b

FIG. 18A

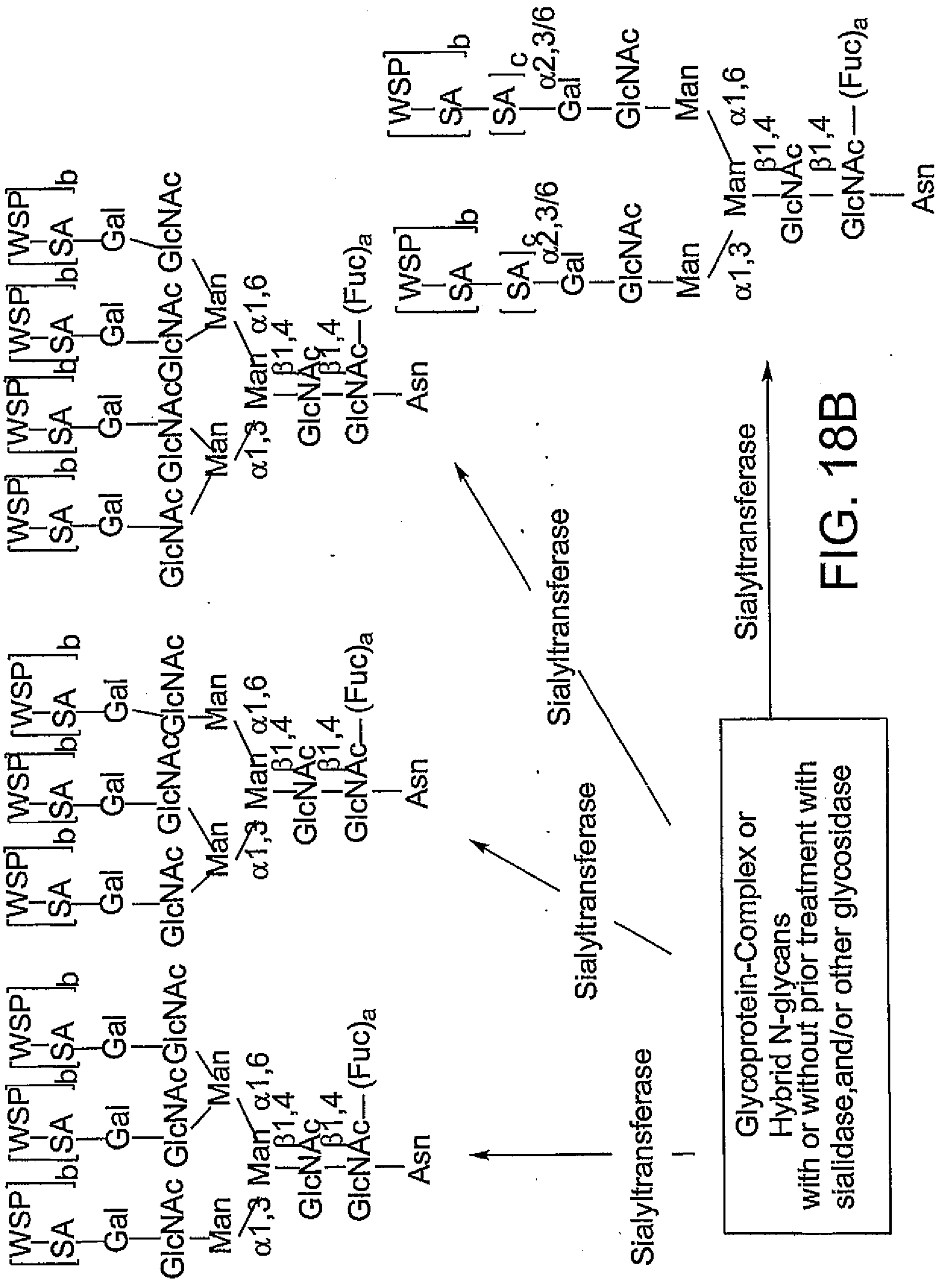

Glycoprotein-Complex or Hybrid N-glycans with or without prior treatment with sialidase,and/or other glycosidase
Sialyltransferase
Sialyltransferase
Sialyltransferase
Sialyltransferase
WSP
SA
Gal
GlcNAc
Man
α1,3
α1,6
β1,4
GlcNAc
Asn
(Fuc)a
SA
c
α2,3/6
b

FIG. 18B

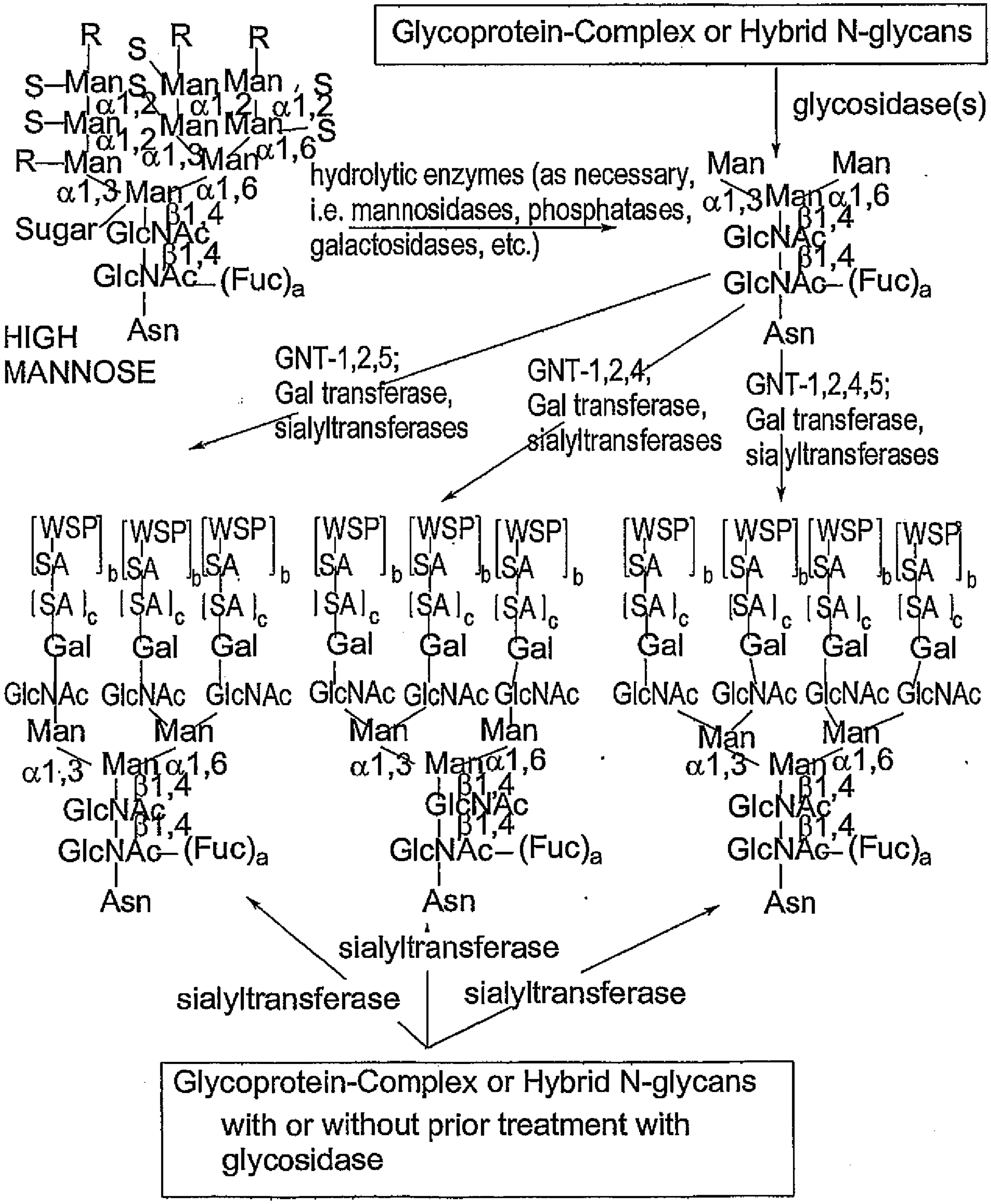

Glycoprotein-Complex or Hybrid N-glycans
glycosidase(s)
R
S
R
R
S—Man S Man Man S
α1,2 α1,2 α1,2
S—Man Man Man—S
α1,2 α1,3 Man α1,6
R—Man
α1,3 Man α1,6
β1,4
Sugar GlcNAc
β1,4
GlcNAc—(Fuc)a
Asn
HIGH MANNOSE
hydrolytic enzymes (as necessary, i.e. mannosidases, phosphatases, galactosidases, etc.)
Man Man
α1,3 Man α1,6
β1,4
GlcNAc
β1,4
GlcNAc—(Fuc)a
Asn
GNT-1,2,5;
Gal transferase,
sialyltransferases
GNT-1,2,4;
Gal transferase,
sialyltransferases
GNT-1,2,4,5;
Gal transferase,
sialyltransferases
WSP
SA
b
[SA]c
Gal
GlcNAc
Man
α1,3 Man α1,6
β1,4
GlcNAc
β1,4
GlcNAc—(Fuc)a
Asn
sialyltransferase
sialyltransferase
sialyltransferase
Glycoprotein-Complex or Hybrid N-glycans with or without prior treatment with glycosidase

FIG. 19

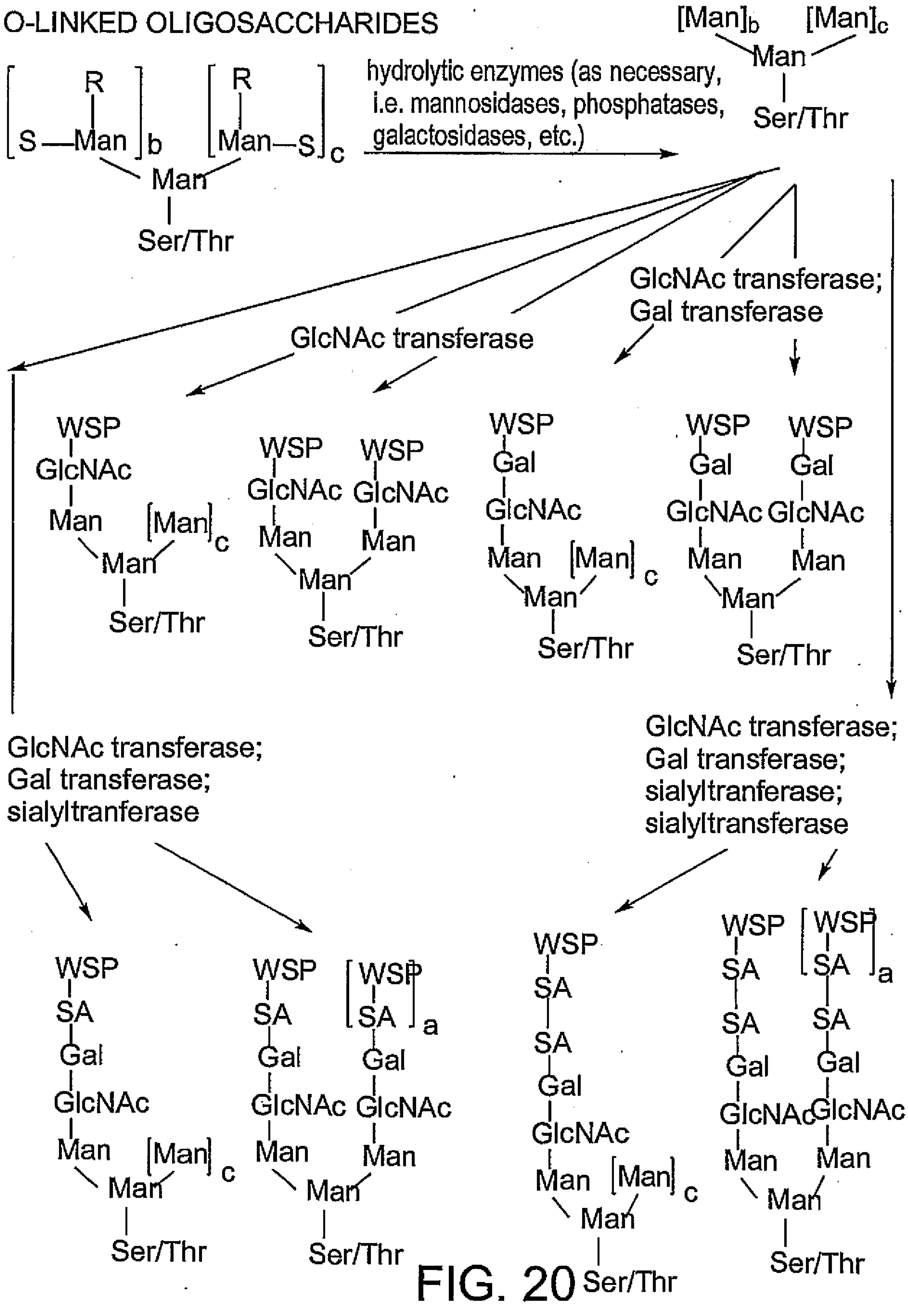

O-LINKED OLIGOSACCHARIDES
R
S—Man
b
R
Man—S
c
Man
Ser/Thr
hydrolytic enzymes (as necessary, i.e. mannosidases, phosphatases, galactosidases, etc.)
[Man]b
[Man]c
Man
Ser/Thr
GlcNAc transferase
GlcNAc transferase; Gal transferase
WSP
GlcNAc
Man
[Man]c
Man
Ser/Thr
WSP
Gal
GlcNAc
GlcNAc transferase; Gal transferase; sialyltranferase
GlcNAc transferase; Gal transferase; sialyltranferase; sialyltransferase
SA
[WSP SA]a

FIG. 20

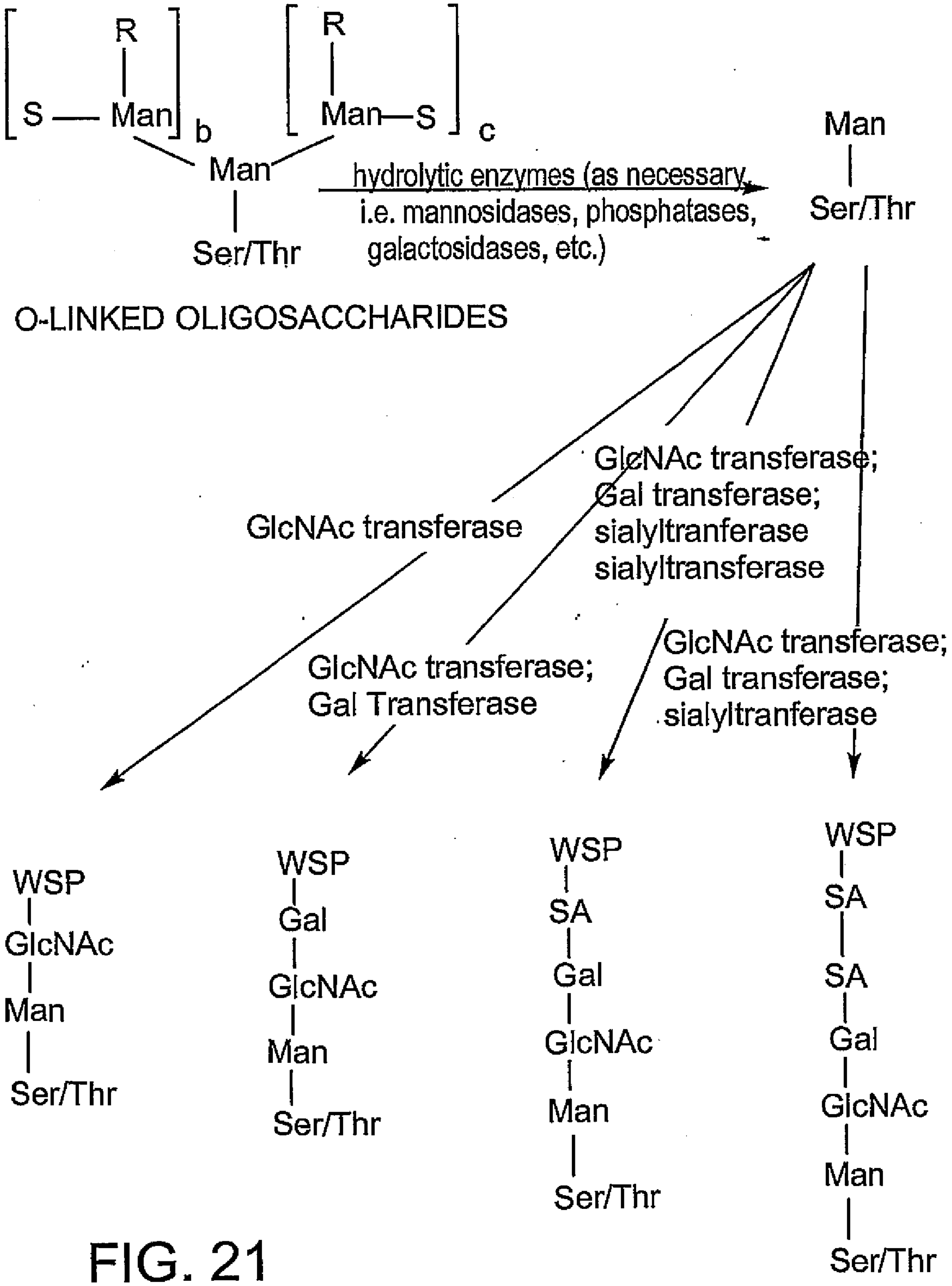

R
S — Man
b
R
Man—S
c
Man
Ser/Thr
hydrolytic enzymes (as necessary,
i.e. mannosidases, phosphatases,
galactosidases, etc.)
Man
Ser/Thr
O-LINKED OLIGOSACCHARIDES
GlcNAc transferase
GlcNAc transferase;
Gal transferase;
sialyltranferase
sialyltransferase
GlcNAc transferase;
Gal Transferase
GlcNAc transferase;
Gal transferase;
sialyltranferase
WSP
GlcNAc
Man
Ser/Thr
WSP
Gal
GlcNAc
Man
Ser/Thr
WSP
SA
Gal
GlcNAc
Man
Ser/Thr
WSP
SA
SA
Gal
GlcNAc
Man
Ser/Thr

FIG. 21

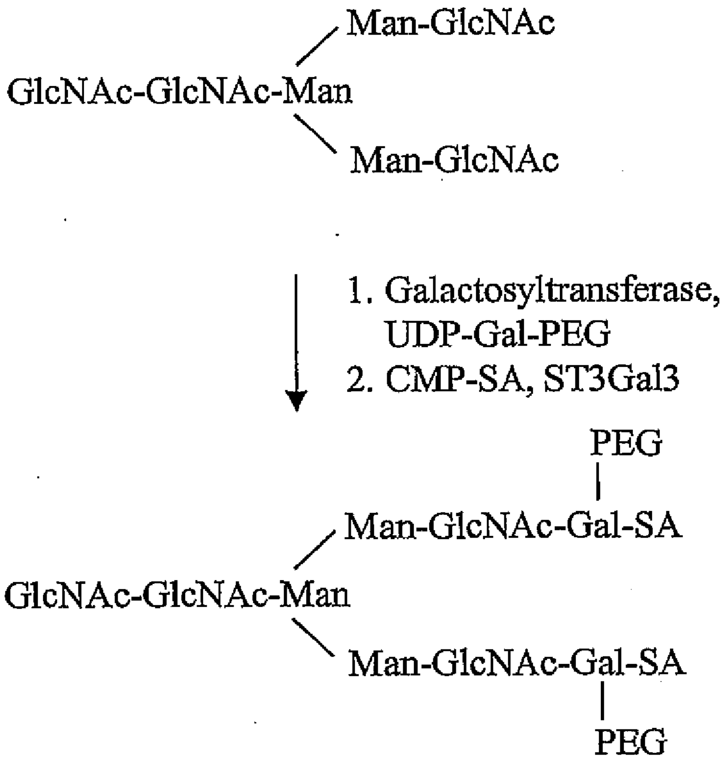

Man-GlcNAc
GlcNAc-GlcNAc-Man
Man-GlcNAc
1. Galactosyltransferase, UDP-Gal-PEG
2. CMP-SA, ST3Gal3
PEG
Man-GlcNAc-Gal-SA
GlcNAc-GlcNAc-Man
Man-GlcNAc-Gal-SA
PEG

FIG. 22A

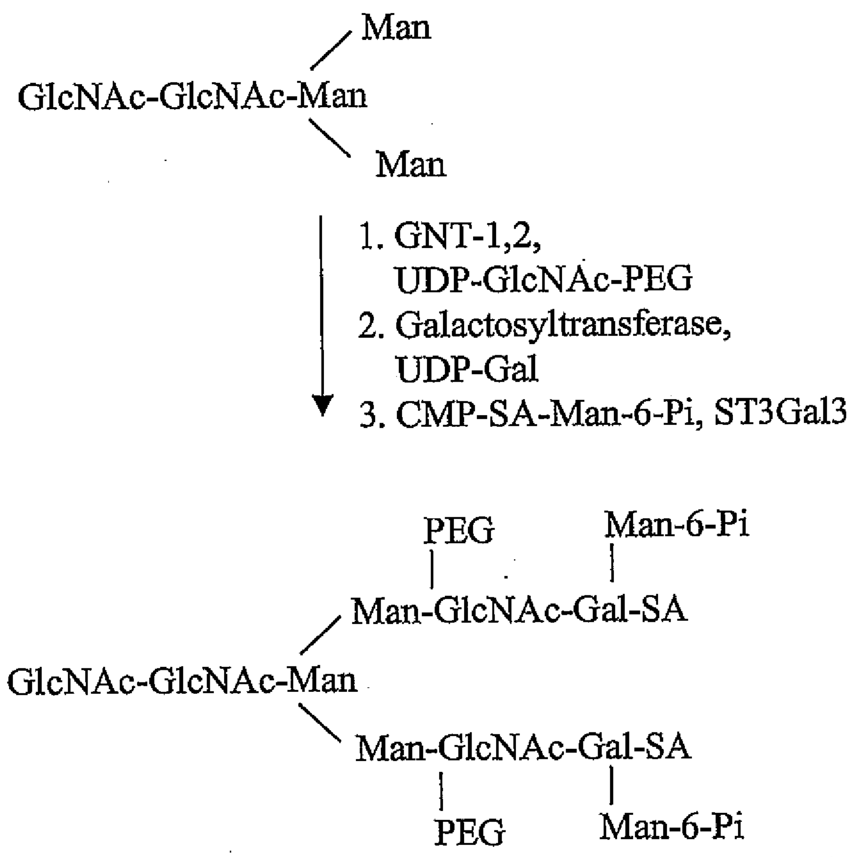

Man
GlcNAc-GlcNAc-Man
Man
1. GNT-1,2, UDP-GlcNAc-PEG
2. Galactosyltransferase, UDP-Gal
3. CMP-SA-Man-6-Pi, ST3Gal3
PEG
Man-6-Pi
Man-GlcNAc-Gal-SA
GlcNAc-GlcNAc-Man
Man-GlcNAc-Gal-SA
PEG
Man-6-Pi

FIG. 22B

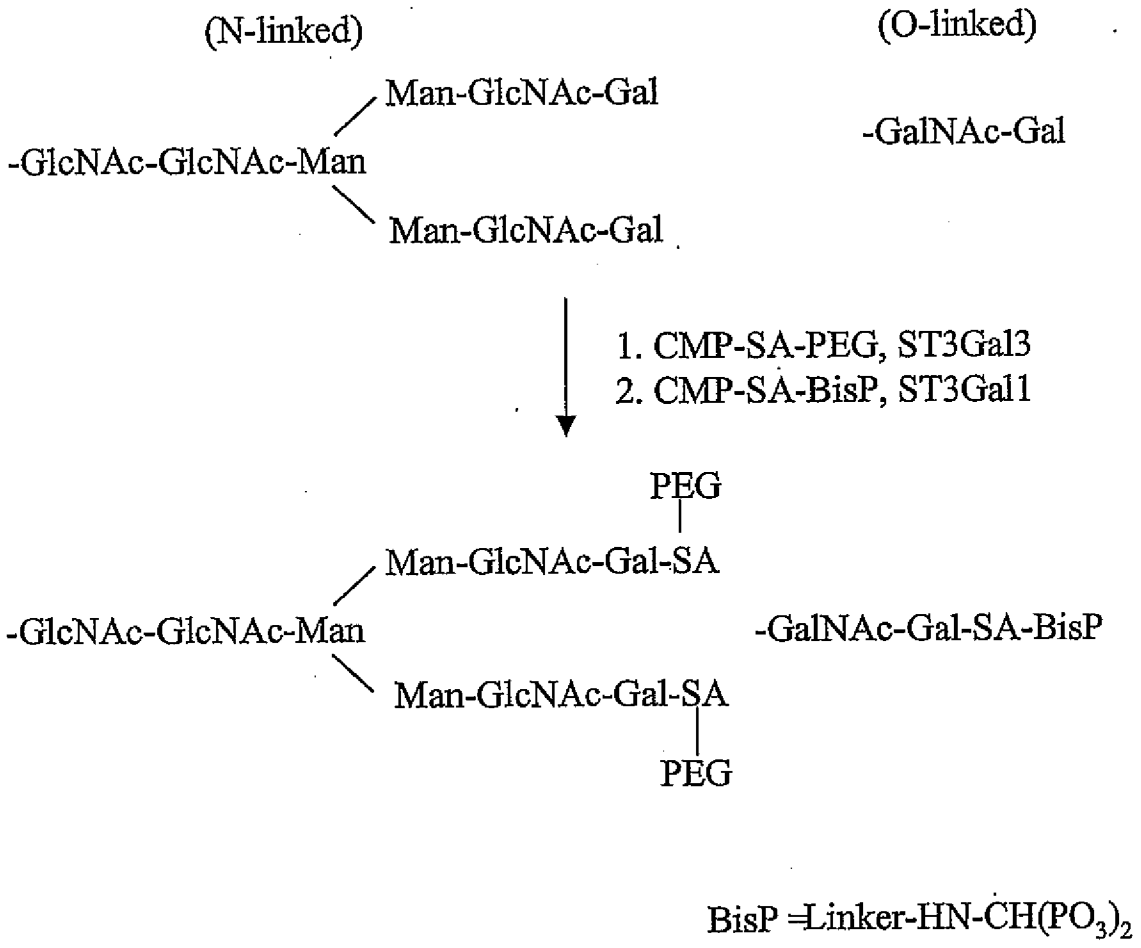

(N-linked)
(O-linked)
Man-GlcNAc-Gal
-GlcNAc-GlcNAc-Man
Man-GlcNAc-Gal
-GalNAc-Gal
1. CMP-SA-PEG, ST3Gal3
2. CMP-SA-BisP, ST3Gal1
PEG
Man-GlcNAc-Gal-SA
-GlcNAc-GlcNAc-Man
Man-GlcNAc-Gal-SA
PEG
-GalNAc-Gal-SA-BisP
BisP =Linker-HN-CH(PO3)2

FIG. 22C

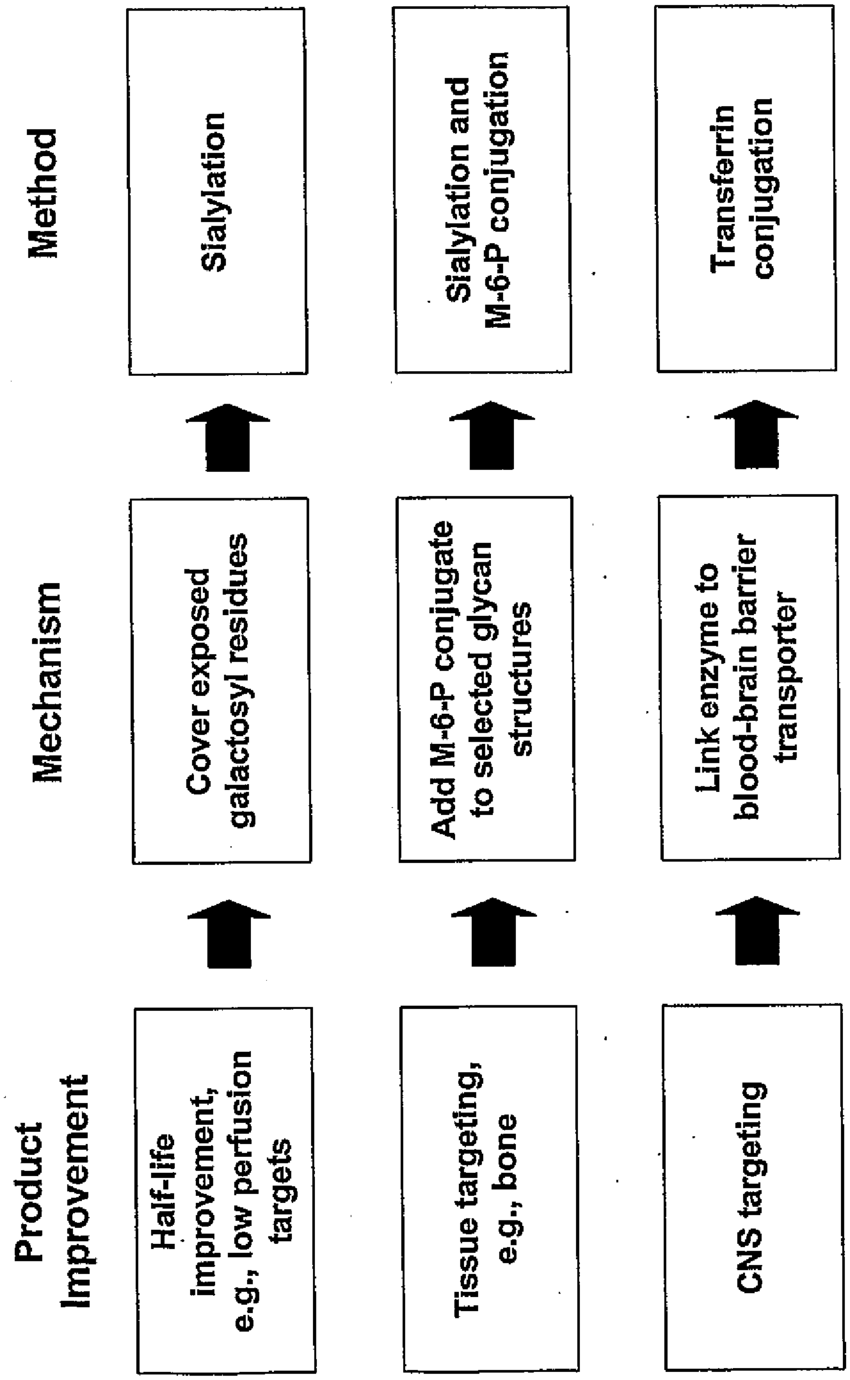

Product Improvement
Mechanism
Method
Half-life improvement, e.g., low perfusion targets
Cover exposed galactosyl residues
Sialylation
Tissue targeting, e.g., bone
Add M-6-P conjugate to selected glycan structures
Sialylation and M-6-P conjugation
CNS targeting
Link enzyme to blood-brain barrier transporter
Transferrin conjugation

FIG. 23

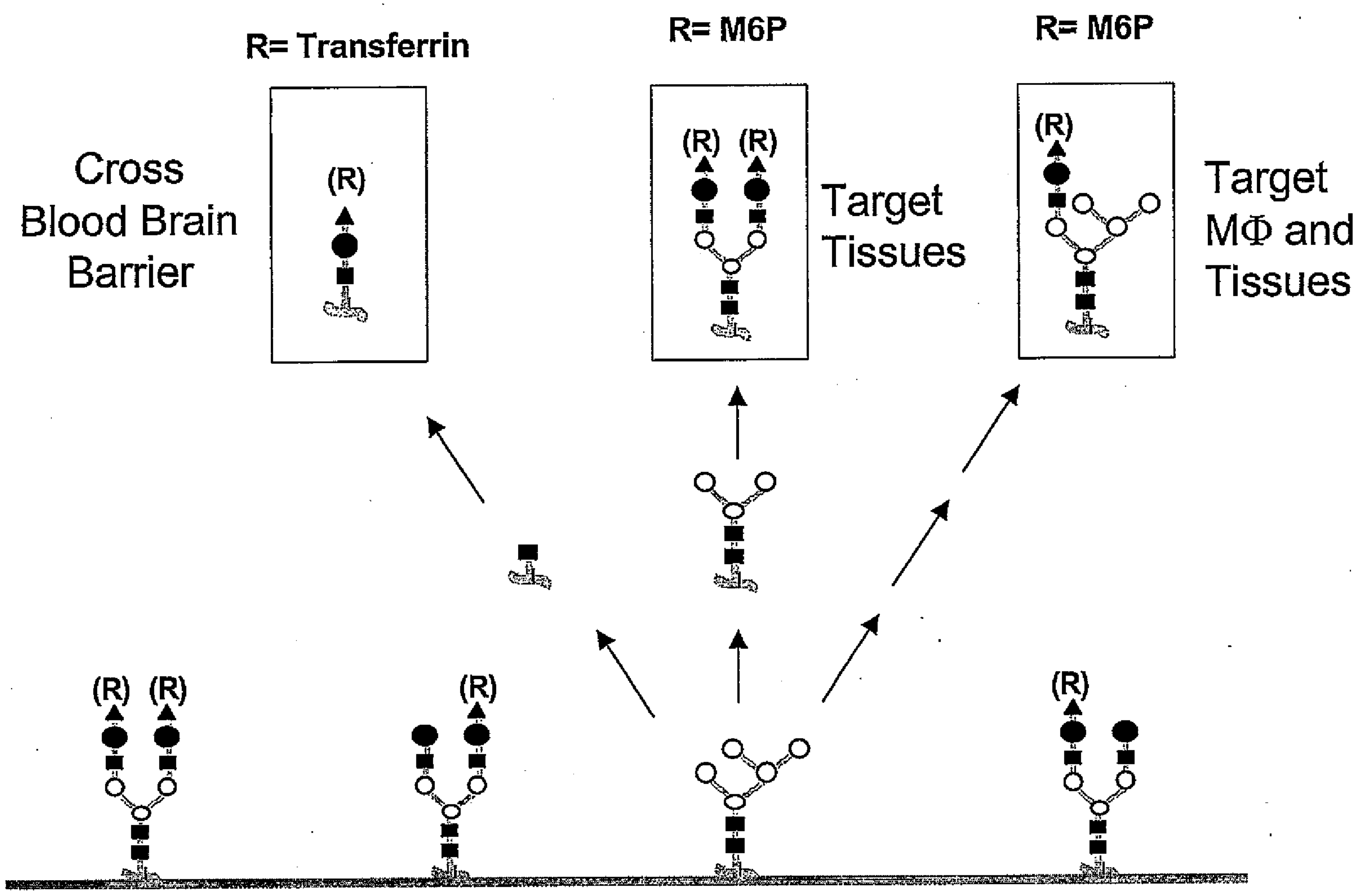

R= Transferrin
R= M6P
R= M6P
Cross
Blood Brain
Barrier
Target
Tissues
Target
MΦ and
Tissues
(R)
(R)

FIG. 24

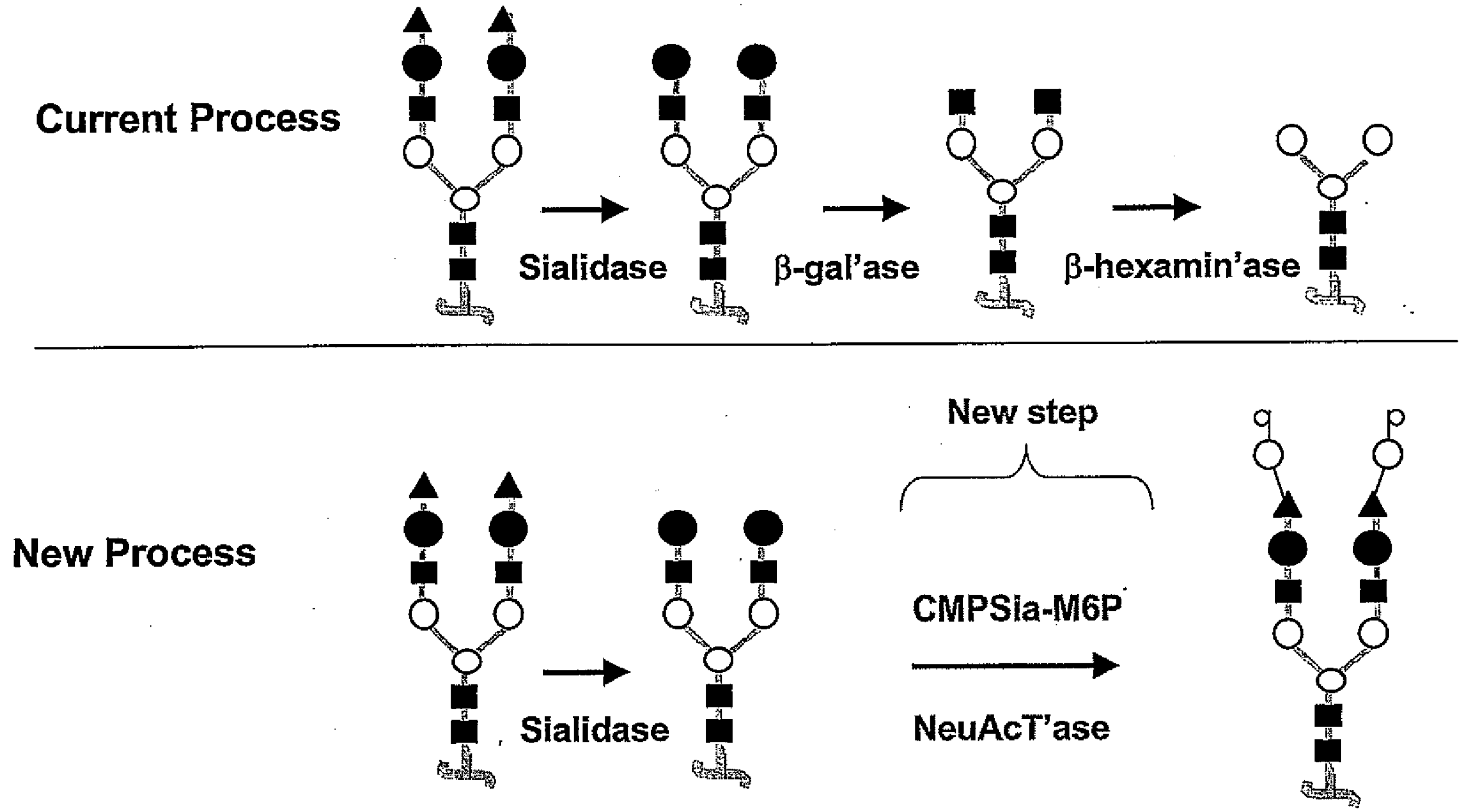

Current Process
Sialidase
β-gal'ase
β-hexamin'ase
New Process
Sialidase
New step
CMPSia-M6P
NeuAcT'ase

FIG. 25

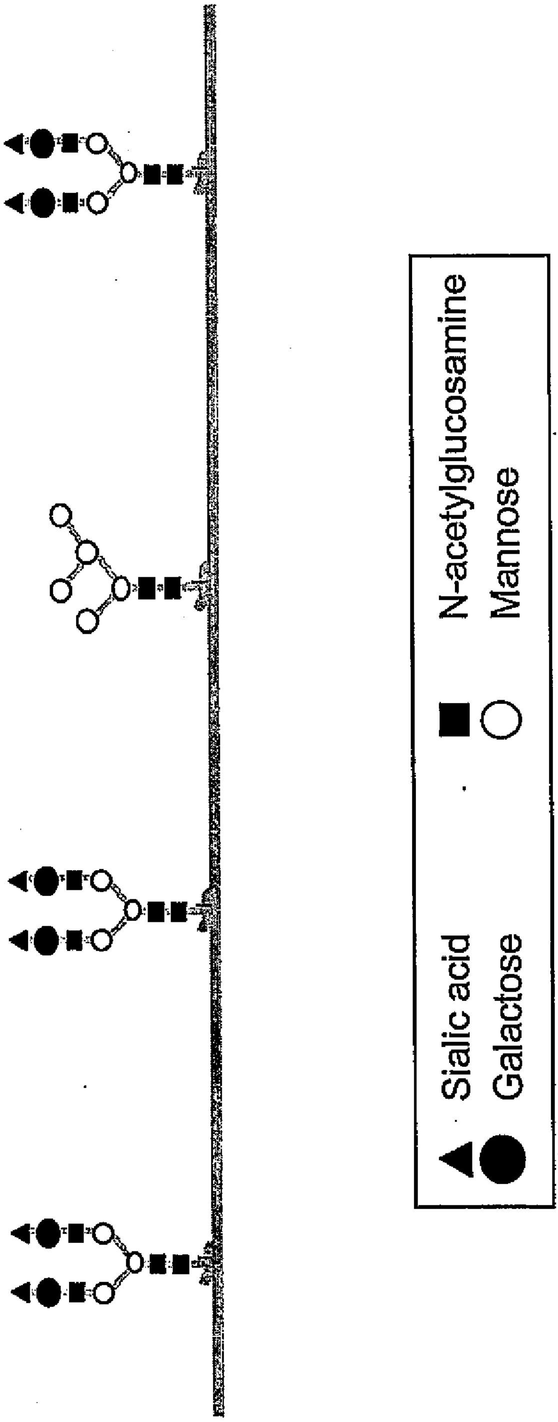
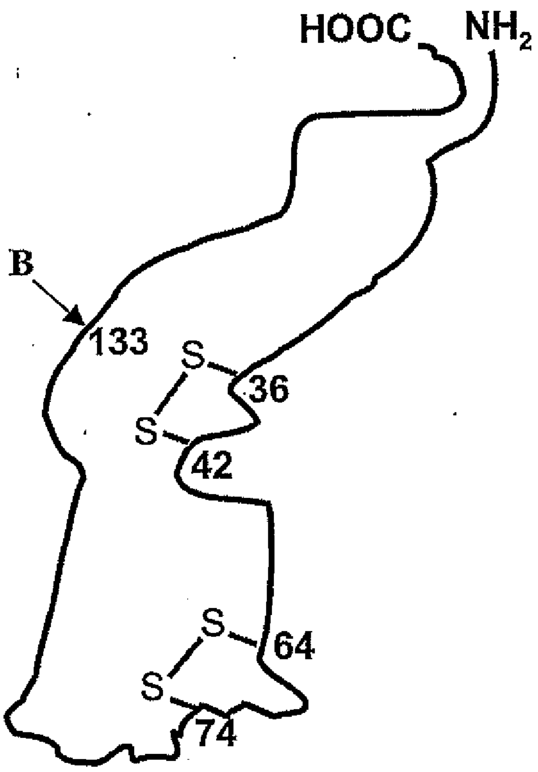
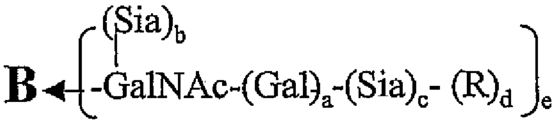


FIG. 26





$$\mathbf{B} \leftarrow \left[-\overset{(\text{Sia})_b}{\text{GalNAc}}-(\text{Gal})_a-(\text{Sia})_c-(\text{R})_d \right]_e$$

a-c, e (independently selected) = 0 or 1;
d = 0;
R = modifying group, mannose, oligomannose

FIG. 27A

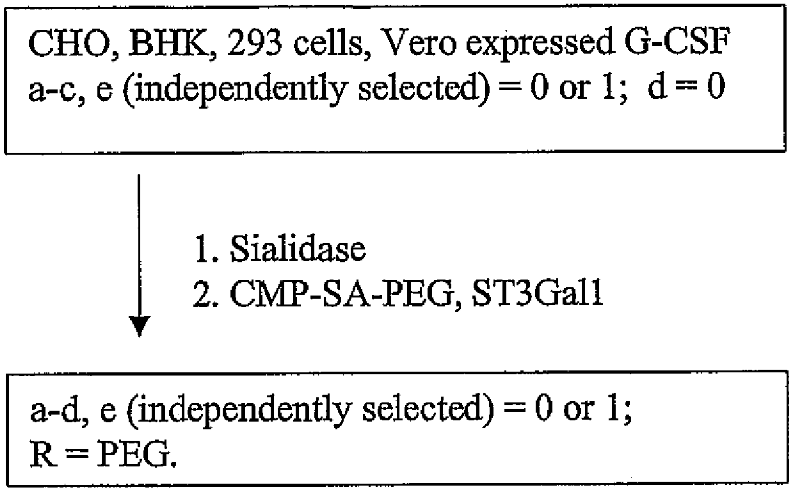

CHO, BHK, 293 cells, Vero expressed G-CSF
a-c, e (independently selected) = 0 or 1; d = 0
1. Sialidase
2. CMP-SA-PEG, ST3Gal1
a-d, e (independently selected) = 0 or 1;
R = PEG.

FIG. 27B

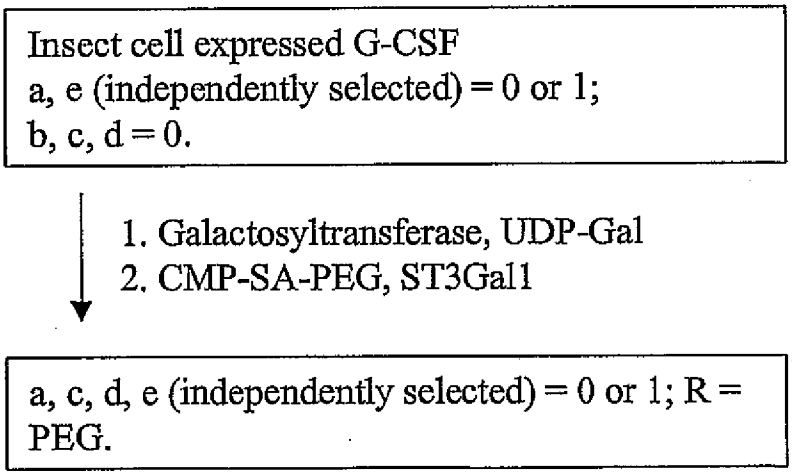

Insect cell expressed G-CSF
a, e (independently selected) = 0 or 1;
b, c, d = 0.
1. Galactosyltransferase, UDP-Gal
2. CMP-SA-PEG, ST3Gal1
a, c, d, e (independently selected) = 0 or 1; R = PEG.

FIG. 27C

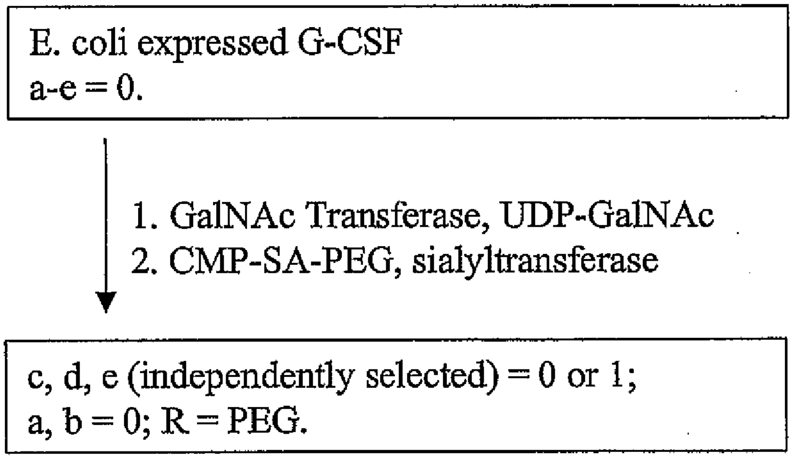

E. coli expressed G-CSF
a-e = 0.
1. GalNAc Transferase, UDP-GalNAc
2. CMP-SA-PEG, sialyltransferase
c, d, e (independently selected) = 0 or 1;
a, b = 0; R = PEG.

FIG. 27D

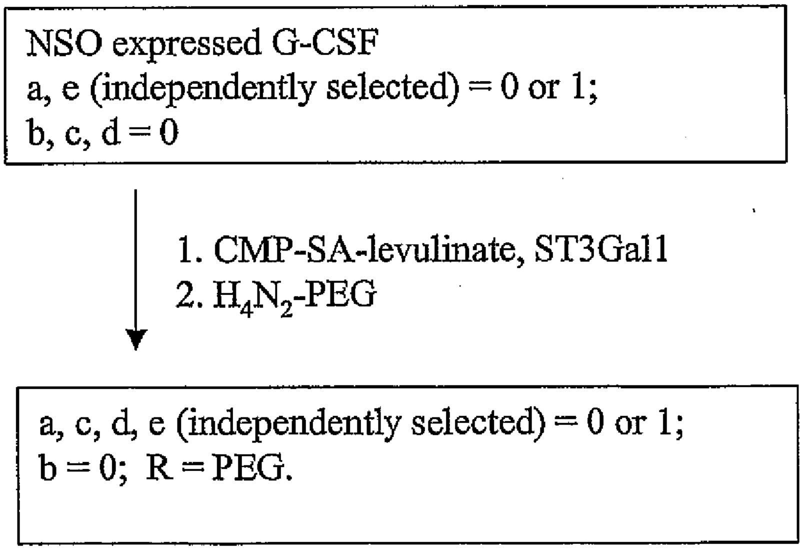

NSO expressed G-CSF
a, e (independently selected) = 0 or 1;
b, c, d = 0
1. CMP-SA-levulinate, ST3Gal1
2. H_4N_2-PEG
a, c, d, e (independently selected) = 0 or 1;
b = 0; R = PEG.

FIG. 27E

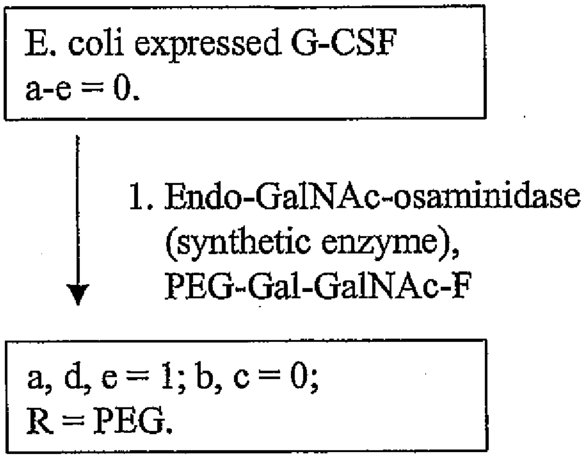


FIG. 27F

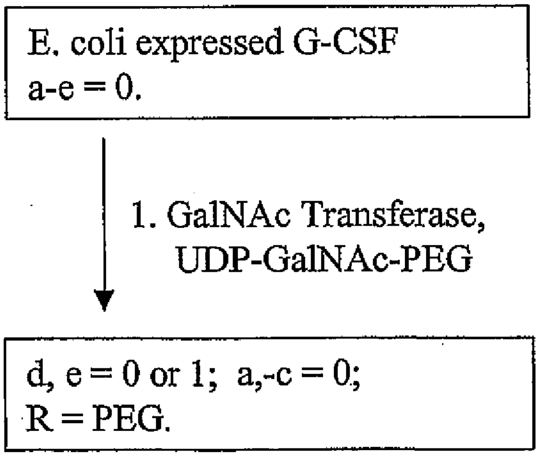
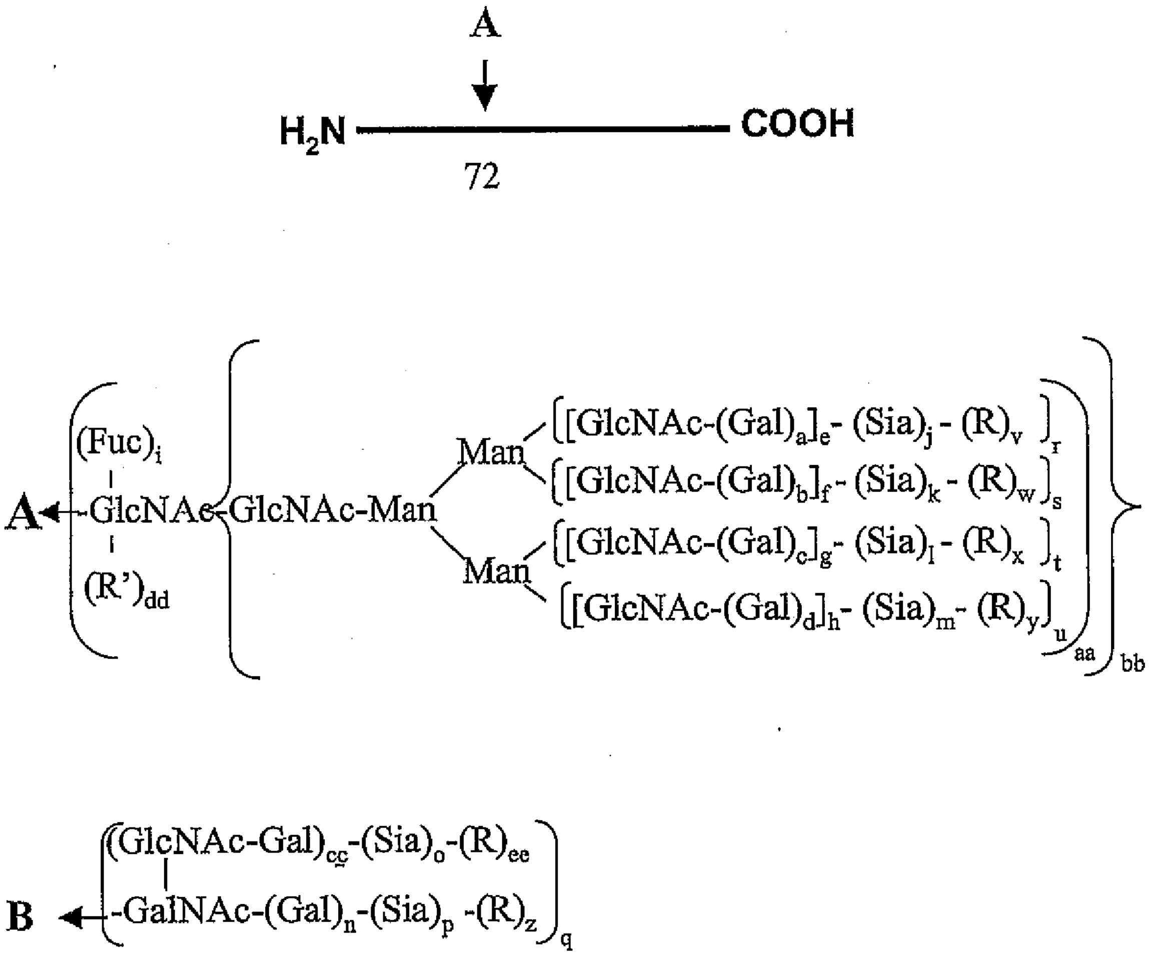


FIG. 27G


A
H2N
COOH
72
A
(Fuc)i
GlcNAc
(R')dd
GlcNAc-Man
Man
Man
[[GlcNAc-(Gal)a]e- (Sia)j - (R)v]r
[[GlcNAc-(Gal)b]f - (Sia)k - (R)w]s
[[GlcNAc-(Gal)c]g- (Sia)l - (R)x]t
[[GlcNAc-(Gal)d]h- (Sia)m- (R)y]u
aa
bb
B
(GlcNAc-Gal)cc-(Sia)o-(R)ee
-GalNAc-(Gal)n-(Sia)p -(R)z
q

a-d, i, n-u (independently selected) = 0 or 1.
aa, bb, cc, dd, ee (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 20.
v-z = 0; R = modifying group, mannose, oligo-mannose.
R' = H, glycosyl residue, modifying group,
glycoconjugate.

FIG. 28A

CHO, BHK, 293 cells, Vero expressed
interferon alpha 14C.
a-d, aa, bb = 1; e-h = 1 to 4;
cc, j-m, i, r-u (independently selected) = 0 or 1;
q, n-p, v-z, cc, dd, ee = 0.

↓

1. Sialidase
2. CMP-SA-PEG, ST3Gal3

a-d, aa, bb = 1; e-h = 1 to 4;
bb, cc, i, r-u (independently selected) = 0 or 1;
q, n-p, v-z, cc, dd, ee = 0;
v-y (independently selected) = 1,
when j-m (independently selected) = 1;
R = PEG.

FIG. 28B

Insect cell or fungi expressed interferon alpha-14C.
a-d, f, h, j-q, s, u, v-z, cc, dd, ee = 0;
e, g, i, r, t (independently selected) = 0 or 1;
aa, bb = 1.

↓

1. GNT's 1&2, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal-PEG

b, d, f, h, j-q, s, u, w, y, z, cc, dd, ee = 0;
a, c, e, g, i, r, t, v, x (independently selected) = 0 or 1;
v, x (independently selected) = 1,
when a, c, (independently selected) = 1;
aa, bb = 1; R = PEG.

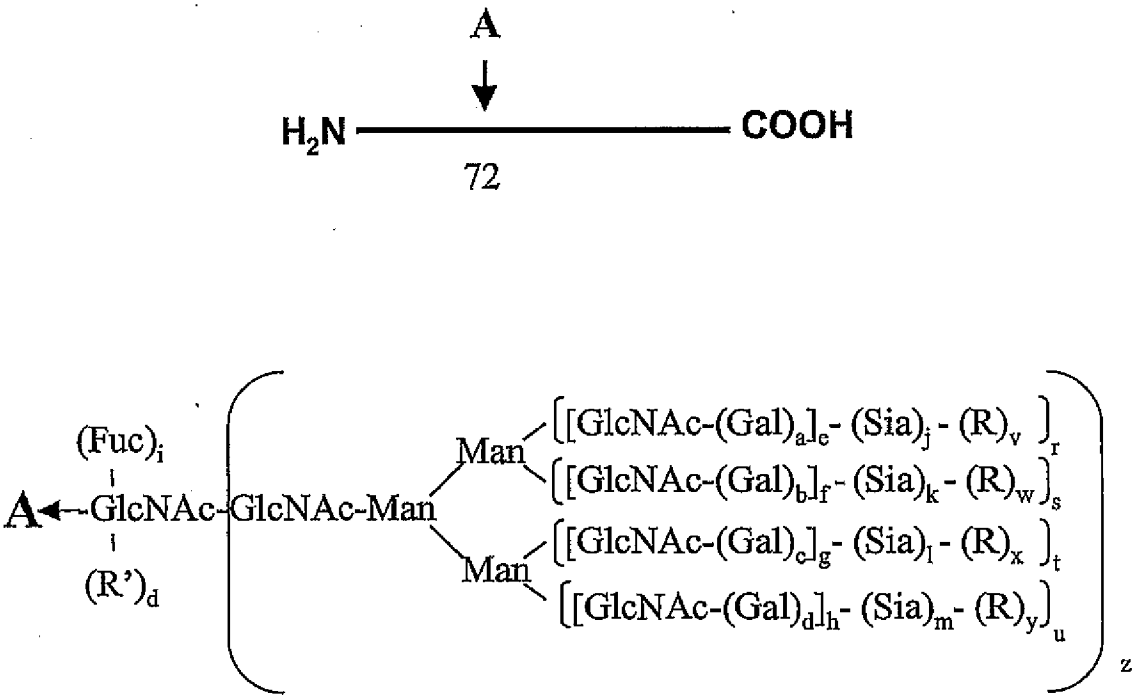
FIG. 28C

Yeast expressed interferon alpha-14C.
a-q, cc, dd, ee, v-z = 0;
r-y (independently selected) = 0 to 1;
aa, bb = 1;
R (branched or linear) = Man, oligomannose or polysaccharide.

1. Endo-H
2. Galactosyltransferase, UDP-Gal
3.. CMP-SA-PEG, ST3Gal3

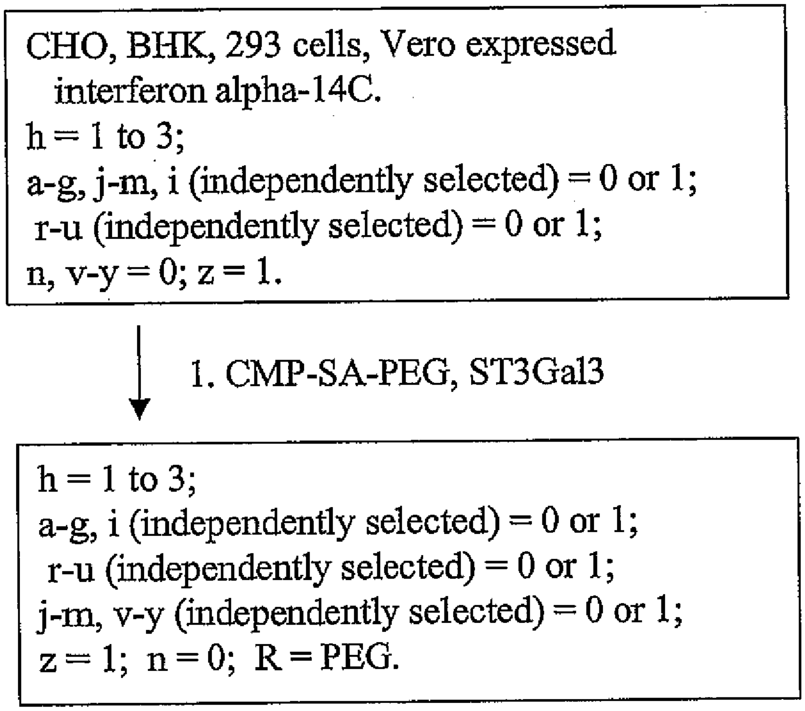
a-z, bb = 0; aa = 1; R' = -Gal-Sia-PEG.

FIG. 28D


A
H2N
COOH
72
(Fuc)i
A
GlcNAc-GlcNAc-Man
(R')d
Man
[[GlcNAc-(Gal)a]e- (Sia)j - (R)v]r
[[GlcNAc-(Gal)b]f - (Sia)k - (R)w]s
Man
[[GlcNAc-(Gal)c]g- (Sia)l - (R)x]t
[[GlcNAc-(Gal)d]h- (Sia)m- (R)y]u
z

a-d, i, r-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
j-m (independently selected) = 0 or 1.
n, v-y = 0; z = 0 or 1.
R = polymer; R' = sugar, glycoconjugate.

FIG. 28E

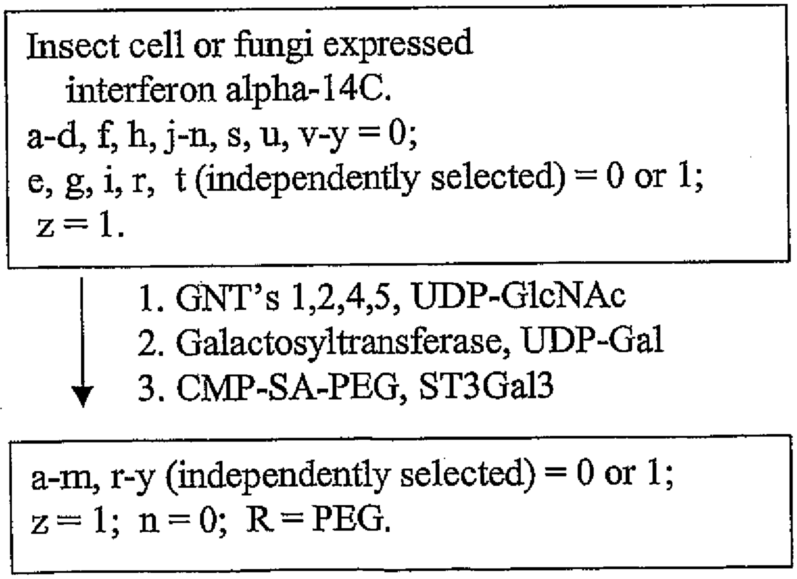


CHO, BHK, 293 cells, Vero expressed interferon alpha-14C.
h = 1 to 3;
a-g, j-m, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
n, v-y = 0; z = 1.

1. CMP-SA-PEG, ST3Gal3

h = 1 to 3;
a-g, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
j-m, v-y (independently selected) = 0 or 1;
z = 1; n = 0; R = PEG.

FIG. 28F



Insect cell or fungi expressed interferon alpha-14C.
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, r, t (independently selected) = 0 or 1;
z = 1.

1. GNT's 1,2,4,5, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal
3. CMP-SA-PEG, ST3Gal3

a-m, r-y (independently selected) = 0 or 1;
z = 1; n = 0; R = PEG.

FIG. 28G

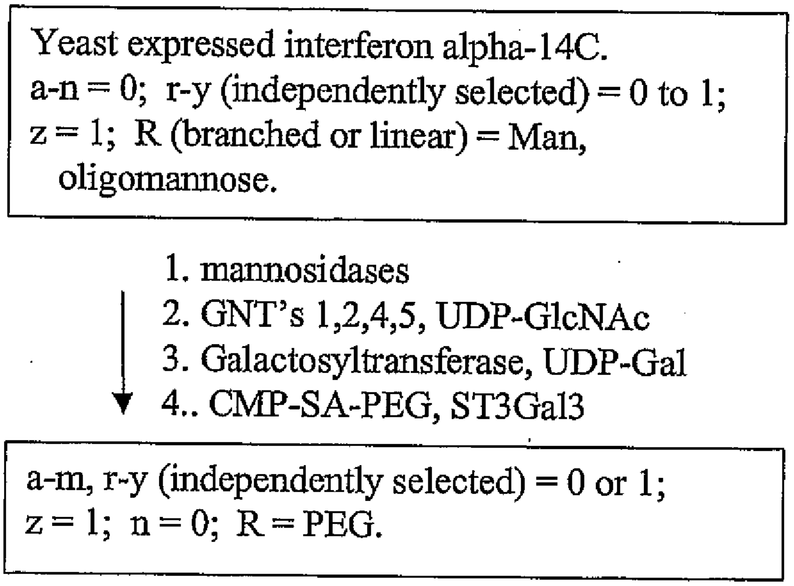

Yeast expressed interferon alpha-14C.
a-n = 0; r-y (independently selected) = 0 to 1;
z = 1; R (branched or linear) = Man, oligomannose.
1. mannosidases
2. GNT's 1,2,4,5, UDP-GlcNAc
3. Galactosyltransferase, UDP-Gal
4.. CMP-SA-PEG, ST3Gal3
a-m, r-y (independently selected) = 0 or 1;
z = 1; n = 0; R = PEG.

FIG. 28H

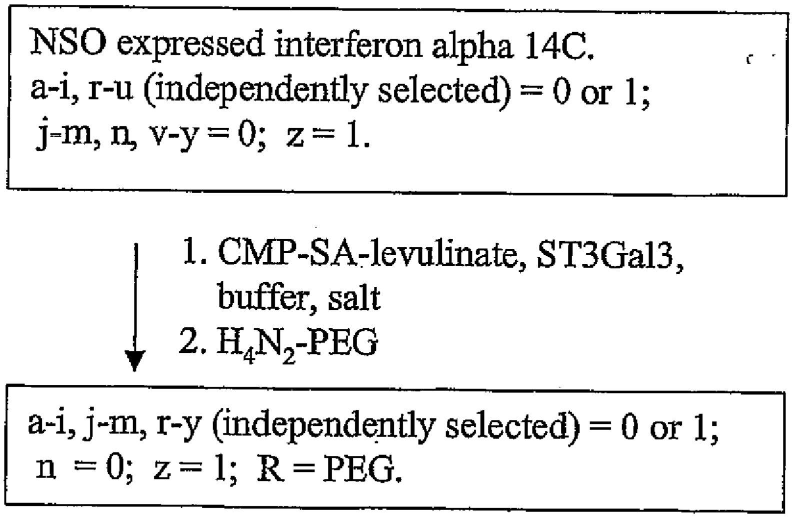
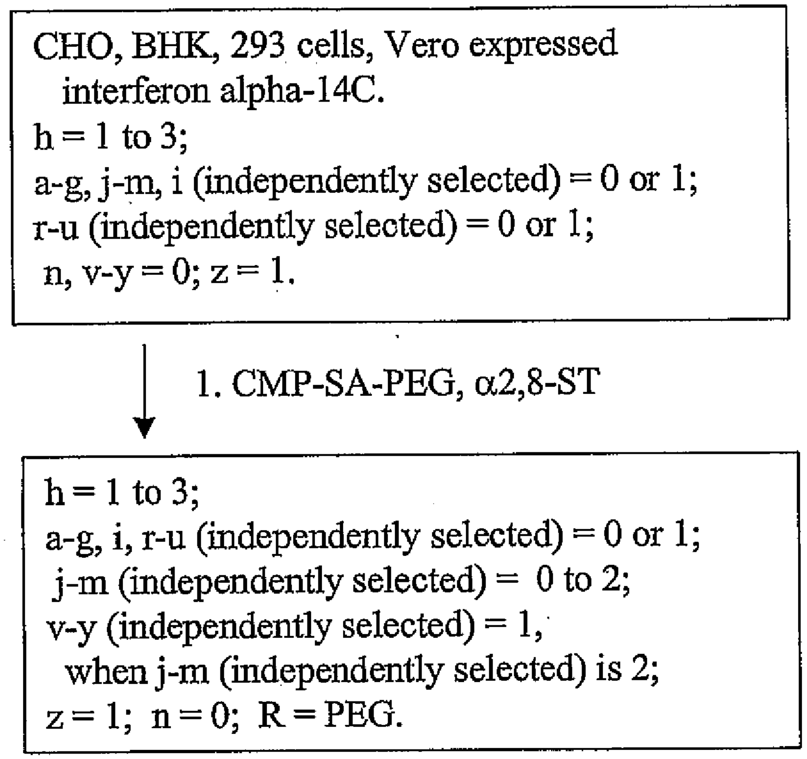

NSO expressed interferon alpha 14C.
a-i, r-u (independently selected) = 0 or 1;
j-m, n, v-y = 0; z = 1.
1. CMP-SA-levulinate, ST3Gal3, buffer, salt
2. H_4N_2-PEG
a-i, j-m, r-y (independently selected) = 0 or 1;
n = 0; z = 1; R = PEG.

FIG. 28I

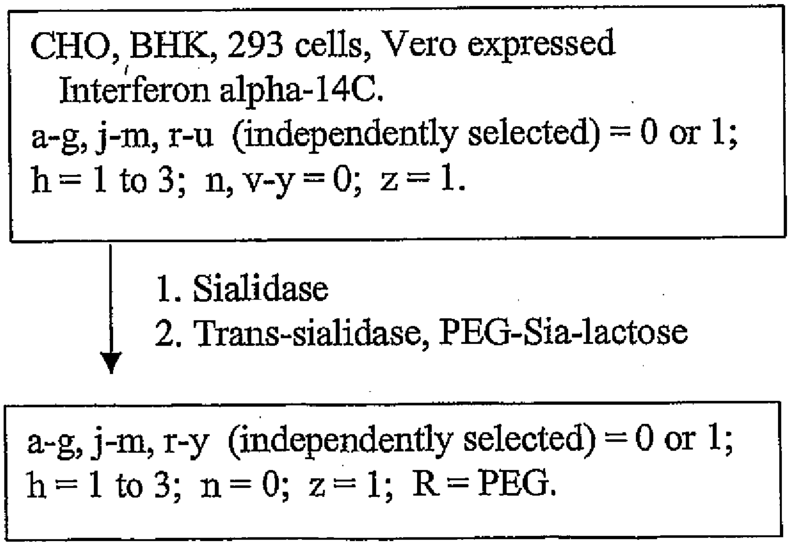


CHO, BHK, 293 cells, Vero expressed interferon alpha-14C.
h = 1 to 3;
a-g, j-m, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
n, v-y = 0; z = 1.

1. CMP-SA-PEG, α2,8-ST

h = 1 to 3;
a-g, i, r-u (independently selected) = 0 or 1;
j-m (independently selected) = 0 to 2;
v-y (independently selected) = 1,
when j-m (independently selected) is 2;
z = 1; n = 0; R = PEG.

FIG. 28J

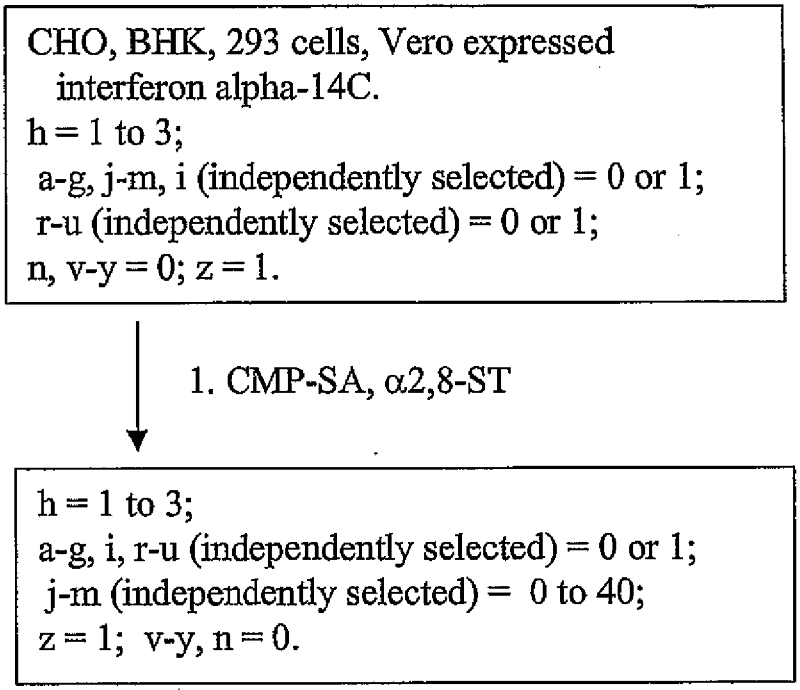


CHO, BHK, 293 cells, Vero expressed Interferon alpha-14C.
a-g, j-m, r-u (independently selected) = 0 or 1;
h = 1 to 3; n, v-y = 0; z = 1.

1. Sialidase
2. Trans-sialidase, PEG-Sia-lactose

a-g, j-m, r-y (independently selected) = 0 or 1;
h = 1 to 3; n = 0; z = 1; R = PEG.

FIG. 28K

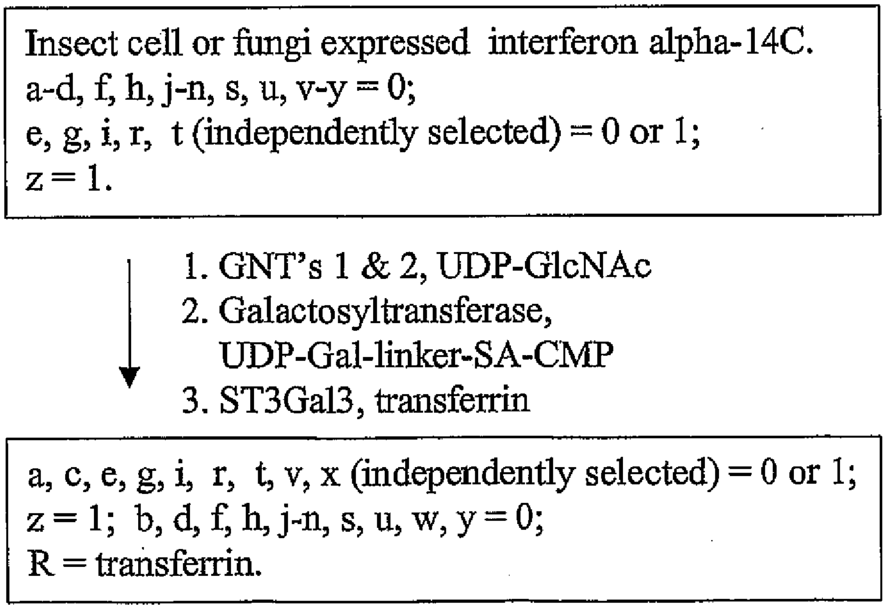


CHO, BHK, 293 cells, Vero expressed interferon alpha-14C.
h = 1 to 3;
a-g, j-m, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
n, v-y = 0; z = 1.

1. CMP-SA, α2,8-ST

h = 1 to 3;
a-g, i, r-u (independently selected) = 0 or 1;
j-m (independently selected) = 0 to 40;
z = 1; v-y, n = 0.

FIG. 28L

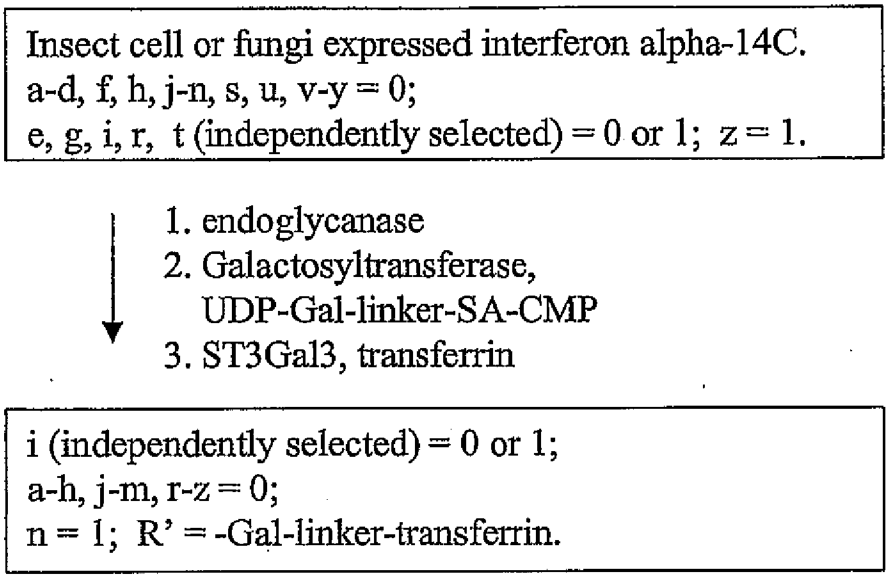


Insect cell or fungi expressed interferon alpha-14C.
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, r, t (independently selected) = 0 or 1;
z = 1.

1. GNT's 1 & 2, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal-linker-SA-CMP
3. ST3Gal3, transferrin

a, c, e, g, i, r, t, v, x (independently selected) = 0 or 1;
z = 1; b, d, f, h, j-n, s, u, w, y = 0;
R = transferrin.

FIG. 28M

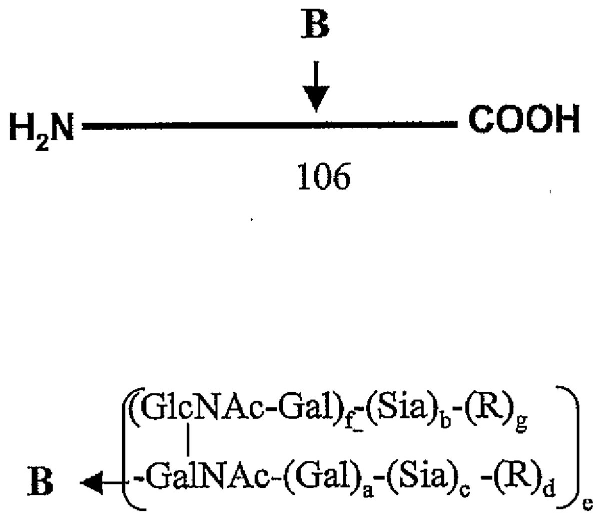


Insect cell or fungi expressed interferon alpha-14C.
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, r, t (independently selected) = 0 or 1; z = 1.

1. endoglycanase
2. Galactosyltransferase, UDP-Gal-linker-SA-CMP
3. ST3Gal3, transferrin

i (independently selected) = 0 or 1;
a-h, j-m, r-z = 0;
n = 1; R' = -Gal-linker-transferrin.

FIG. 28N



$$B \leftarrow \left(\begin{array}{l} (\text{GlcNAc-Gal})_f\text{-}(\text{Sia})_b\text{-}(\text{R})_g \\ \quad\ | \\ \text{-GalNAc-}(\text{Gal})_a\text{-}(\text{Sia})_c\text{-}(\text{R})_d \end{array} \right)_e$$

a-c, e, f (independently selected) = 0 or 1;
d, g = 0; R = polymer, glycoconjugate.

FIG. 28O

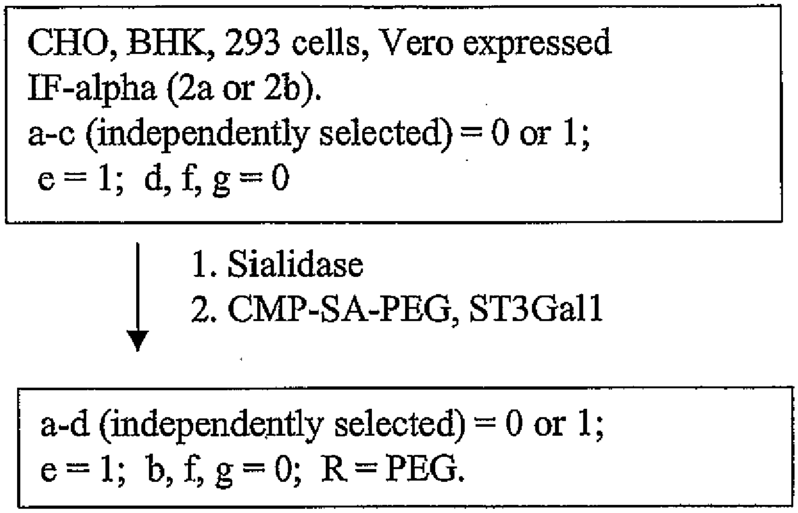

CHO, BHK, 293 cells, Vero expressed IF-alpha (2a or 2b).
a-c (independently selected) = 0 or 1;
e = 1; d, f, g = 0
1. Sialidase
2. CMP-SA-PEG, ST3Gal1
a-d (independently selected) = 0 or 1;
e = 1; b, f, g = 0; R = PEG.

FIG. 28P

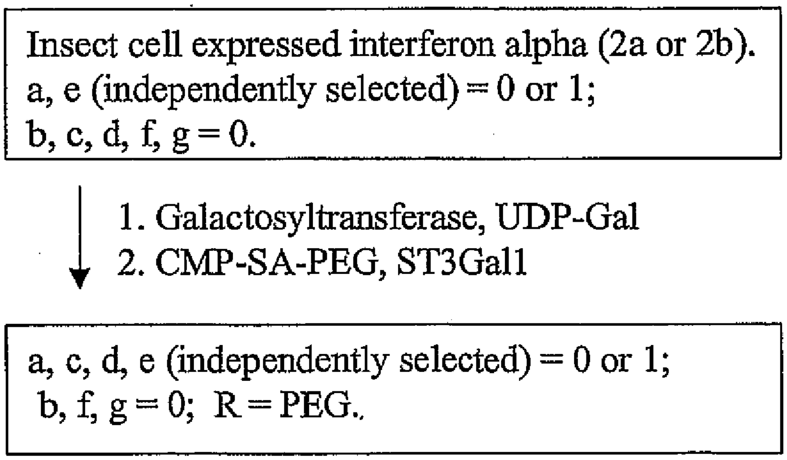

Insect cell expressed interferon alpha (2a or 2b).
a, e (independently selected) = 0 or 1;
b, c, d, f, g = 0.
1. Galactosyltransferase, UDP-Gal
2. CMP-SA-PEG, ST3Gal1
a, c, d, e (independently selected) = 0 or 1;
b, f, g = 0; R = PEG.

FIG. 28Q

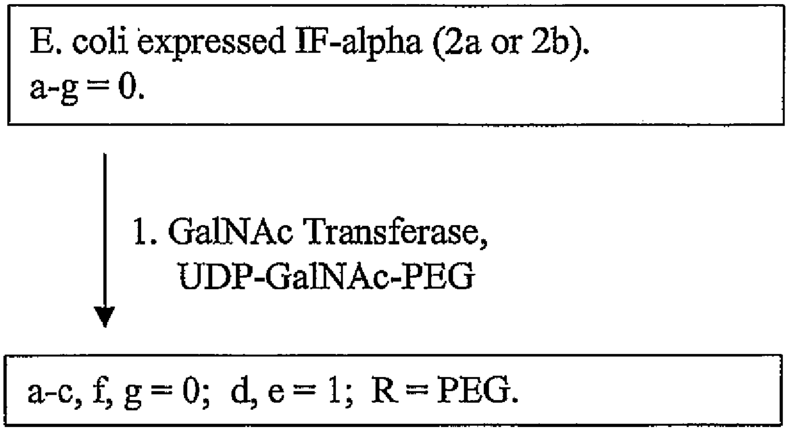

E. coli expressed IF-alpha (2a or 2b).
a-g = 0.
1. GalNAc Transferase, UDP-GalNAc-PEG
a-c, f, g = 0; d, e = 1; R = PEG.

FIG. 28R

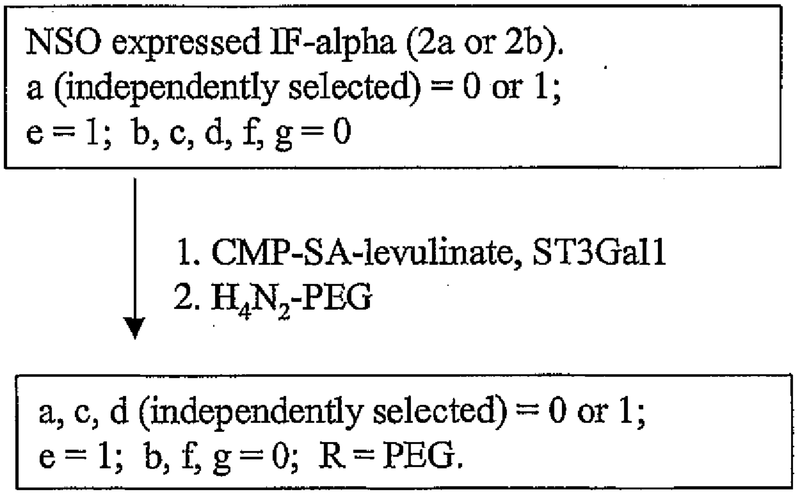

NSO expressed IF-alpha (2a or 2b).
a (independently selected) = 0 or 1;
e = 1; b, c, d, f, g = 0
1. CMP-SA-levulinate, ST3Gal1
2. H_4N_2-PEG
a, c, d (independently selected) = 0 or 1;
e = 1; b, f, g = 0; R = PEG.

FIG. 28S

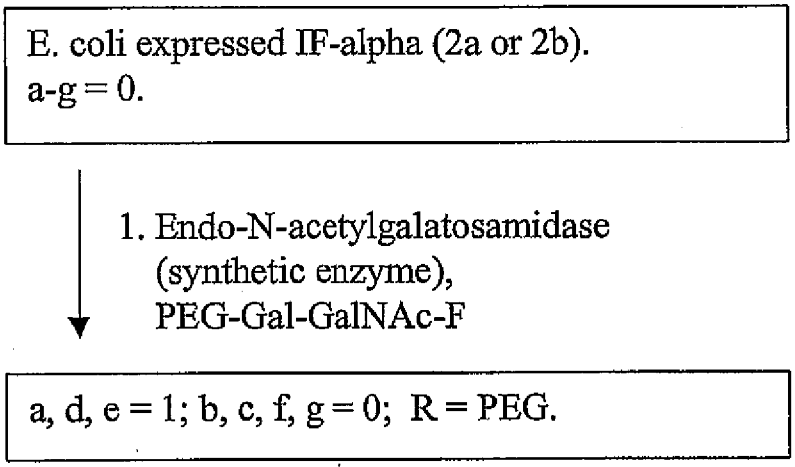

E. coli expressed IF-alpha (2a or 2b).
a-g = 0.
1. Endo-N-acetylgalatosamidase (synthetic enzyme), PEG-Gal-GalNAc-F
a, d, e = 1; b, c, f, g = 0; R = PEG.

FIG. 28T

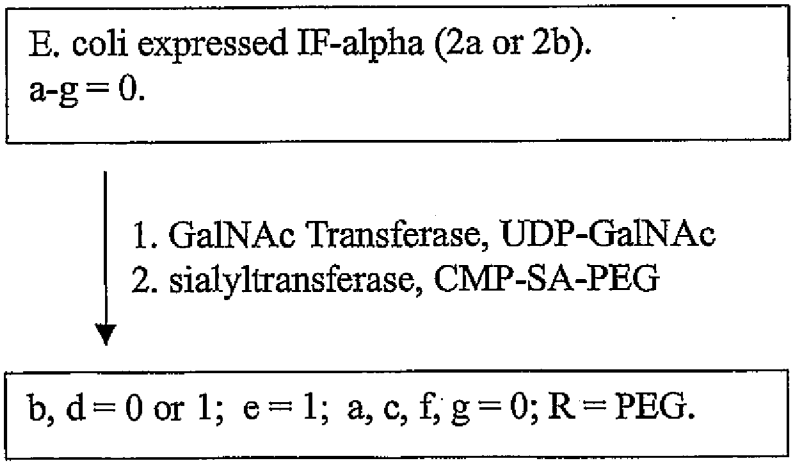

E. coli expressed IF-alpha (2a or 2b).
a-g = 0.
1. GalNAc Transferase, UDP-GalNAc
2. sialyltransferase, CMP-SA-PEG
b, d = 0 or 1; e = 1; a, c, f, g = 0; R = PEG.

FIG. 28U

CHO, BHK, 293 cells, Vero expressed IF-alpha (2a or 2b).
a-c, f (independently selected) = 0 or 1;
e = 1; d, g = 0

↓
1. Sialidase
2. CMP-SA-PEG, ST3Gal1 and ST3Gal3

a-d, f, g (independently selected) = 0 or 1;
e = 1; R = PEG.

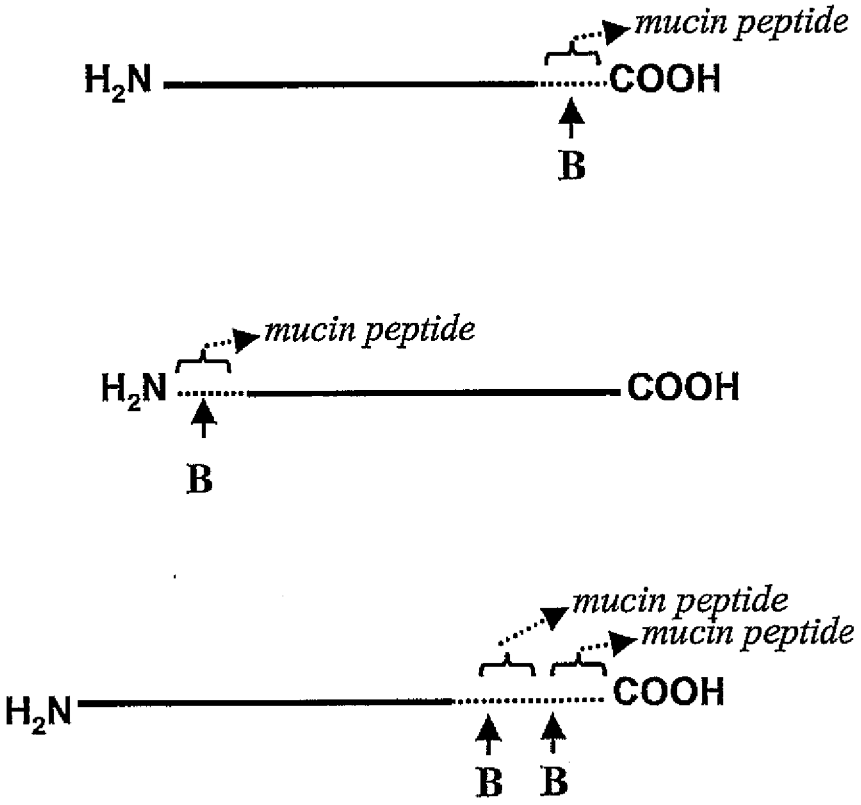
FIG. 28V

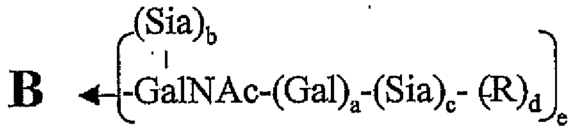
CHO, BHK, 293 cells, Vero expressed
IF-alpha (2a or 2b).
a-c, f (independently selected) = 0 or 1;
e = 1; d, g = 0

↓
1. Sialidase
2. CMP-SA-linker-SA-CMP,
,ST3Gal1
3. ST3Gal3, transferrin

a-d, f (independently selected) = 0 or 1;
e = 1; R = transferrin; g = 0.

FIG. 28W

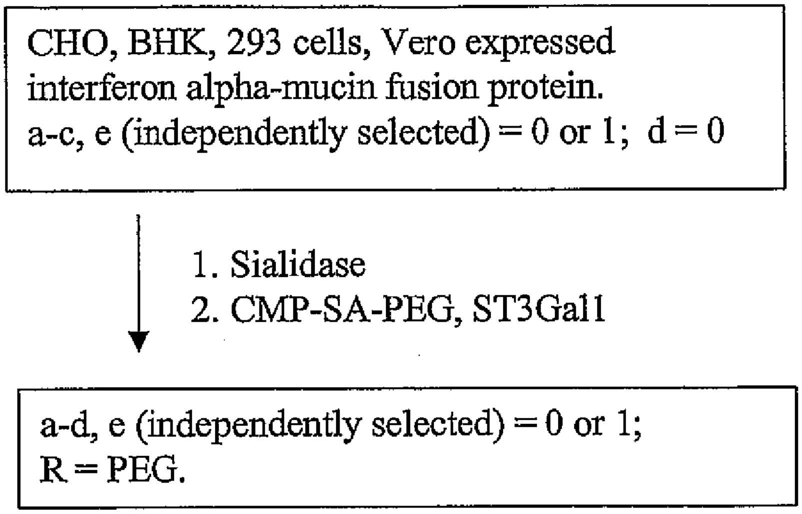




$$\mathbf{B} \leftarrow \left[\overset{(\mathrm{Sia})_b}{\overset{|}{\text{-GalNAc}}}\text{-}(\mathrm{Gal})_a\text{-}(\mathrm{Sia})_c\text{-}(\mathrm{R})_d \right]_e$$

a-c, e (independently selected) = 0 or 1;
d = 0; R = polymer, glycoconjugate.

FIG. 28X

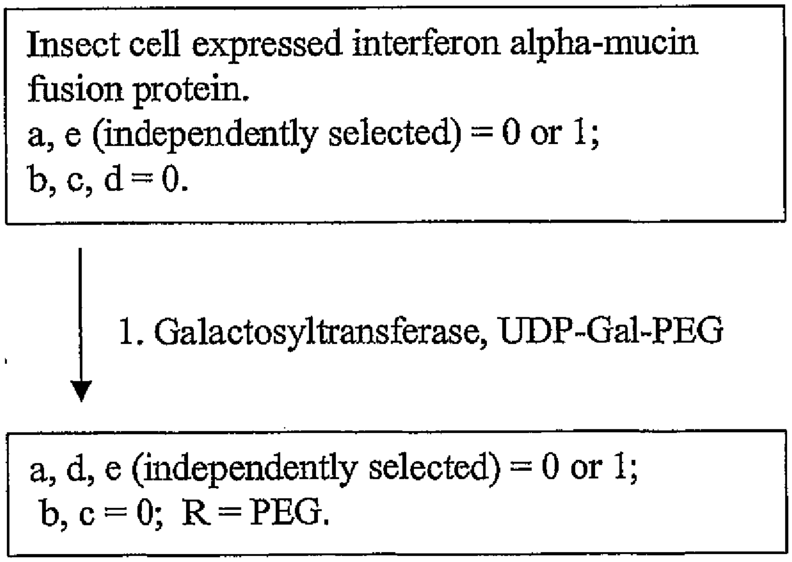


CHO, BHK, 293 cells, Vero expressed interferon alpha-mucin fusion protein.
a-c, e (independently selected) = 0 or 1; d = 0

1. Sialidase
2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1;
R = PEG.

FIG. 28Y



Insect cell expressed interferon alpha-mucin fusion protein.
a, e (independently selected) = 0 or 1;
b, c, d = 0.

1. Galactosyltransferase, UDP-Gal-PEG

a, d, e (independently selected) = 0 or 1;
b, c = 0; R = PEG.

FIG. 28Z

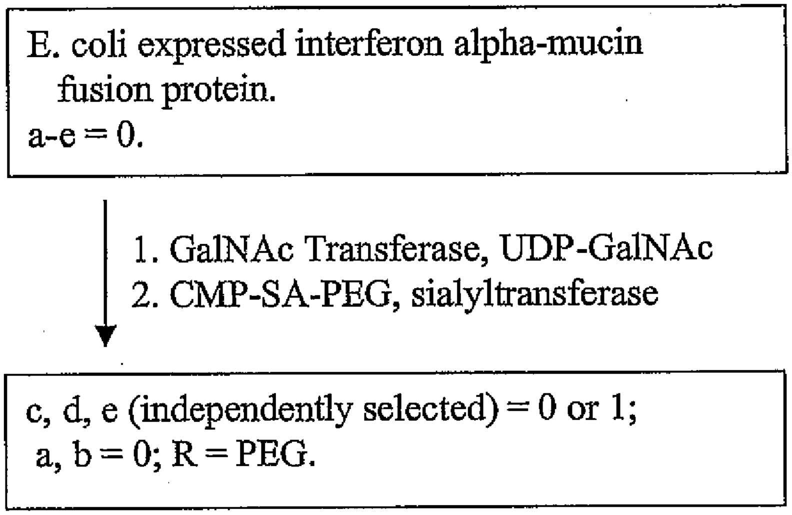
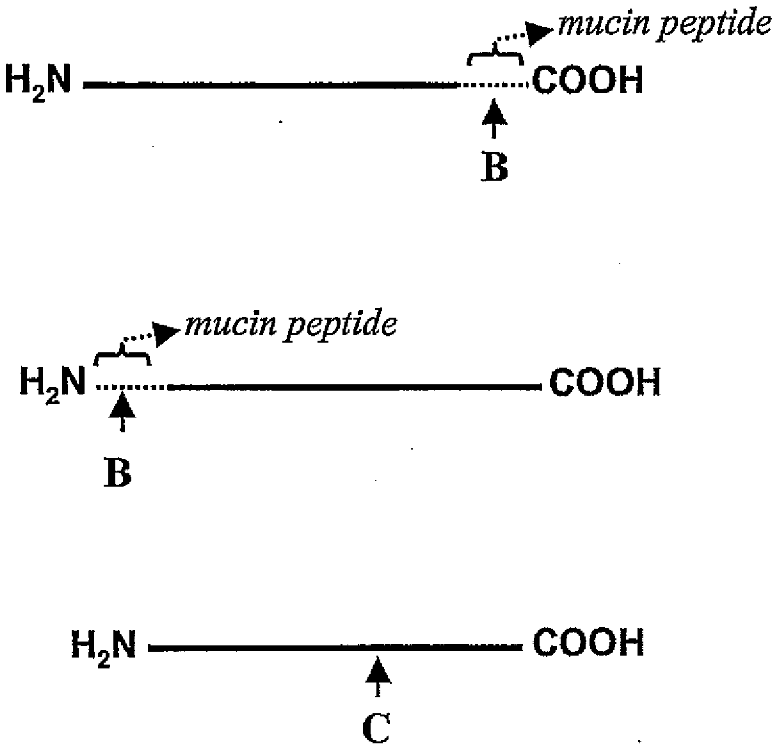
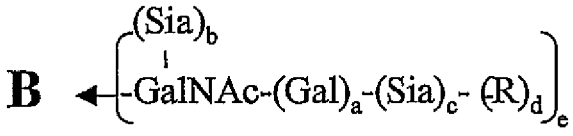

E. coli expressed interferon alpha-mucin fusion protein.
a-e = 0.
1. GalNAc Transferase, UDP-GalNAc
2. CMP-SA-PEG, sialyltransferase
c, d, e (independently selected) = 0 or 1;
a, b = 0; R = PEG.

FIG. 28AA





$$\mathbf{B} \leftarrow \left[\overset{(\mathrm{Sia})_b}{\text{-GalNAc}}\text{-}(\mathrm{Gal})_a\text{-}(\mathrm{Sia})_c\text{-}(\mathrm{R})_d \right]_e$$

$\mathbf{C} \leftarrow (\mathrm{R'})_n$

a-c, e (independently selected) = 0 or 1;
d = 0; R = polymer, linker.

FIG. 28BB

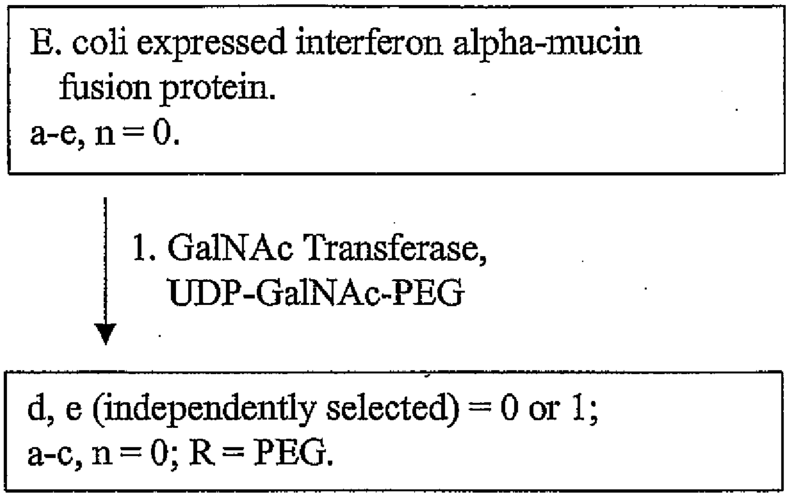

E. coli expressed interferon alpha-mucin fusion protein.
a-e, n = 0.
1. GalNAc Transferase, UDP-GalNAc-PEG
d, e (independently selected) = 0 or 1;
a-c, n = 0; R = PEG.

FIG. 28CC

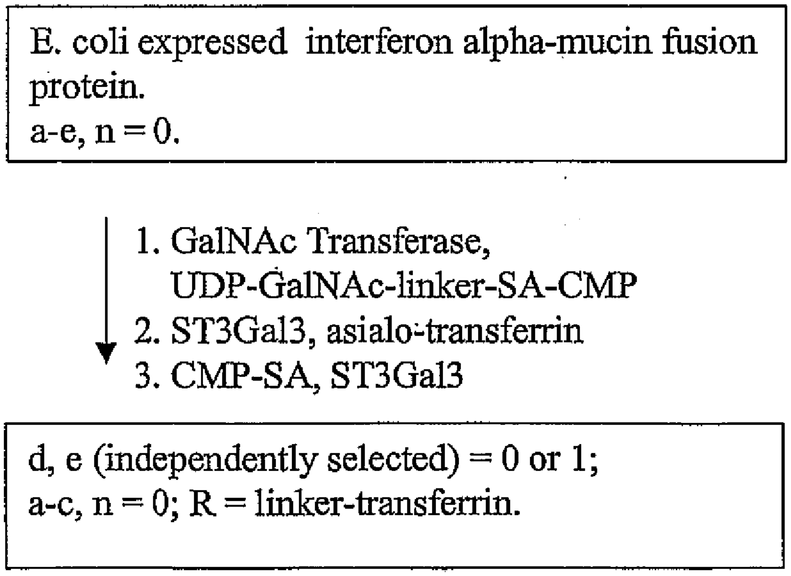

E. coli expressed interferon alpha-mucin fusion protein.
a-e, n = 0.
1. GalNAc Transferase, UDP-GalNAc-linker-SA-CMP
2. ST3Gal3, asialo-transferrin
3. CMP-SA, ST3Gal3
d, e (independently selected) = 0 or 1;
a-c, n = 0; R = linker-transferrin.

FIG. 28DD

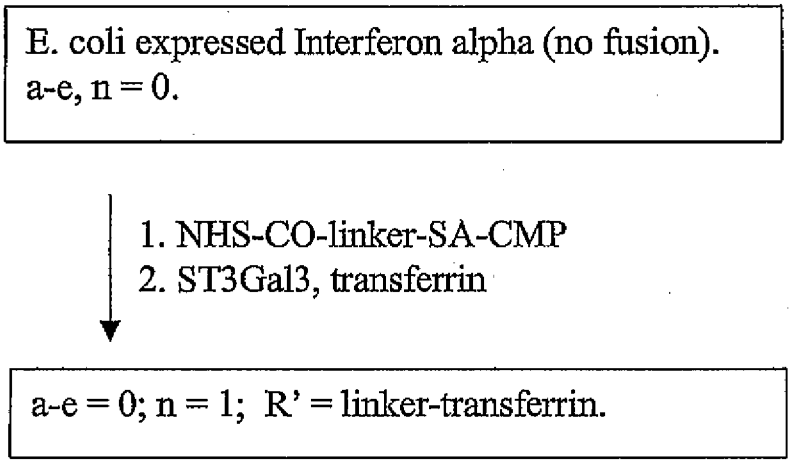
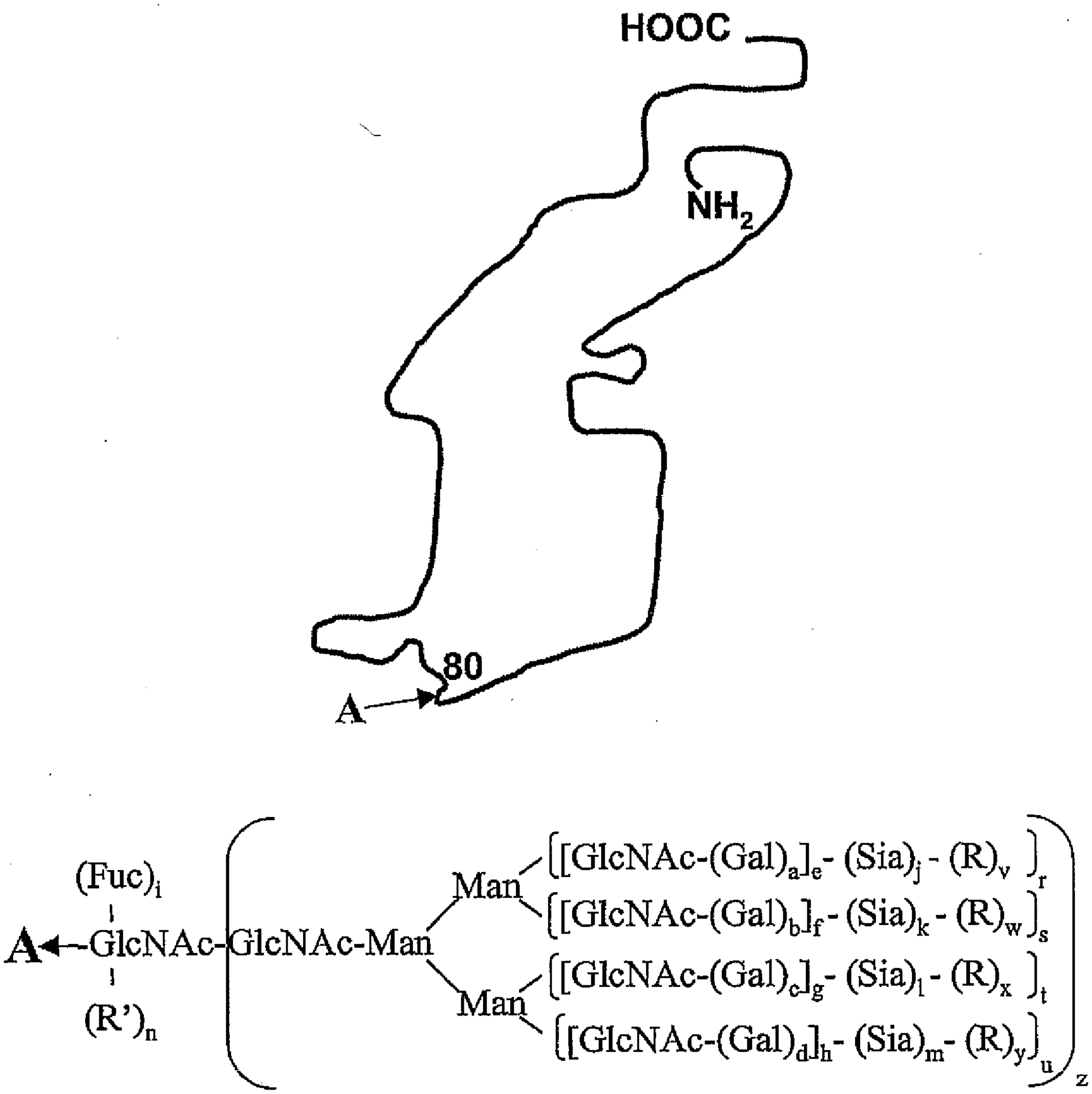
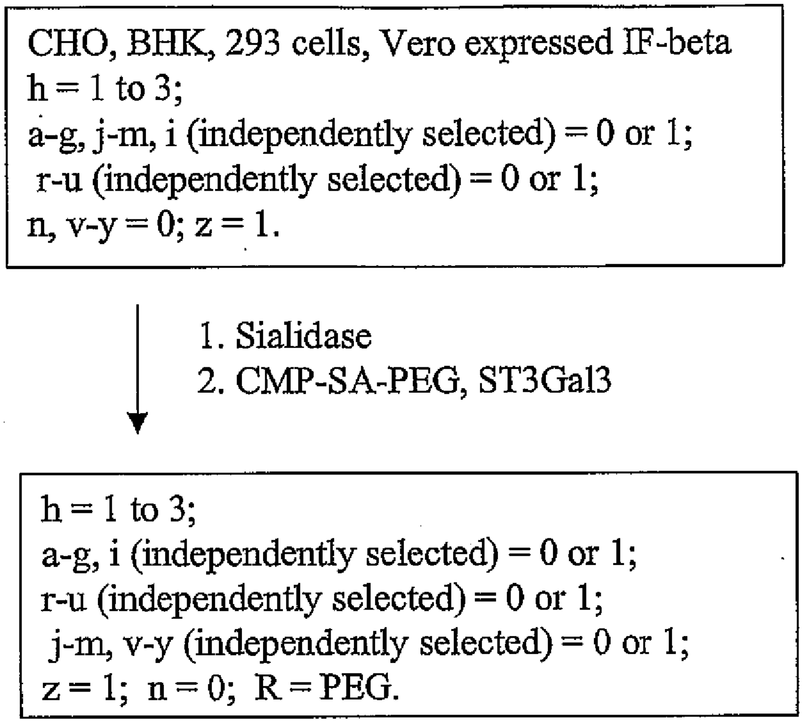

E. coli expressed Interferon alpha (no fusion).
a-e, n = 0.
1. NHS-CO-linker-SA-CMP
2. ST3Gal3, transferrin
a-e = 0; n = 1; R' = linker-transferrin.

FIG. 28EE


HOOC
NH_2
80
A
$(Fuc)_i$
A←GlcNAc-GlcNAc-Man
$(R')_n$
Man
Man
$[[GlcNAc-(Gal)_a]_e-(Sia)_j-(R)_v]_r$
$[[GlcNAc-(Gal)_b]_f-(Sia)_k-(R)_w]_s$
$[[GlcNAc-(Gal)_c]_g-(Sia)_l-(R)_x]_t$
$[[GlcNAc-(Gal)_d]_h-(Sia)_m-(R)_y]_u$
z

a-d, i, r-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
j-m (independently selected) = 0 or 1.
n, v-y = 0; z = 0 or 1; R = polymer

FIG. 29A

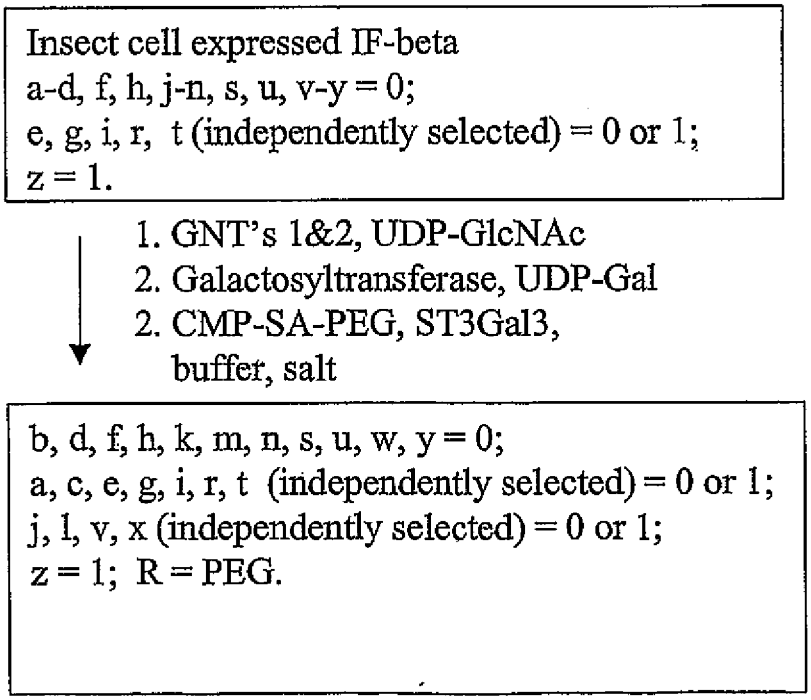


CHO, BHK, 293 cells, Vero expressed IF-beta
h = 1 to 3;
a-g, j-m, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
n, v-y = 0; z = 1.

1. Sialidase
2. CMP-SA-PEG, ST3Gal3

h = 1 to 3;
a-g, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
j-m, v-y (independently selected) = 0 or 1;
z = 1; n = 0; R = PEG.

FIG. 29B



Insect cell expressed IF-beta
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, r, t (independently selected) = 0 or 1;
z = 1.

1. GNT's 1&2, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal
2. CMP-SA-PEG, ST3Gal3,
buffer, salt

b, d, f, h, k, m, n, s, u, w, y = 0;
a, c, e, g, i, r, t (independently selected) = 0 or 1;
j, l, v, x (independently selected) = 0 or 1;
z = 1; R = PEG.

FIG. 29C

Yeast expressed IF-beta
a-n = 0; z = 1;
r-y (independently selected) = 0 to 1;
R (branched or linear) = Man, oligomannose or polysaccharide.

↓
1. Endo-H
2. Galactosyltransferase, UDP-Gal
3.. CMP-SA-PEG, ST3Gal3

a-m, r-z= 0; n = 1; R' = -Gal-Sia-PEG.

FIG. 29D

CHO, BHK, 293 cells, Vero expressed IF-beta
h = 1 to 3;
a-g, j-m, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
n, v-y = 0; z = 1.

↓
1. CMP-SA-PEG, ST3Gal3

h = 1 to 3;
a-g, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
j-m, v-y (independently selected) = 0 or 1;
z = 1; n = 0; R = PEG.

FIG. 29E

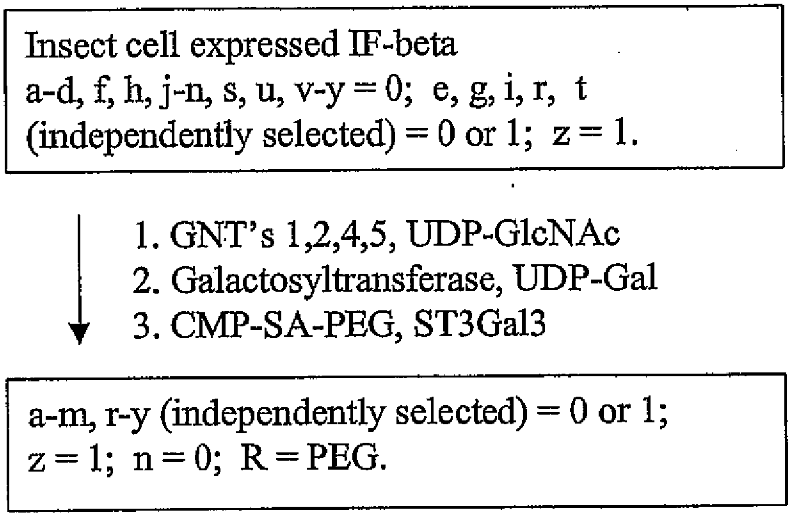

Insect cell expressed IF-beta
a-d, f, h, j-n, s, u, v-y = 0; e, g, i, r, t
(independently selected) = 0 or 1; z = 1.
1. GNT's 1,2,4,5, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal
3. CMP-SA-PEG, ST3Gal3
a-m, r-y (independently selected) = 0 or 1;
z = 1; n = 0; R = PEG.

FIG. 29F

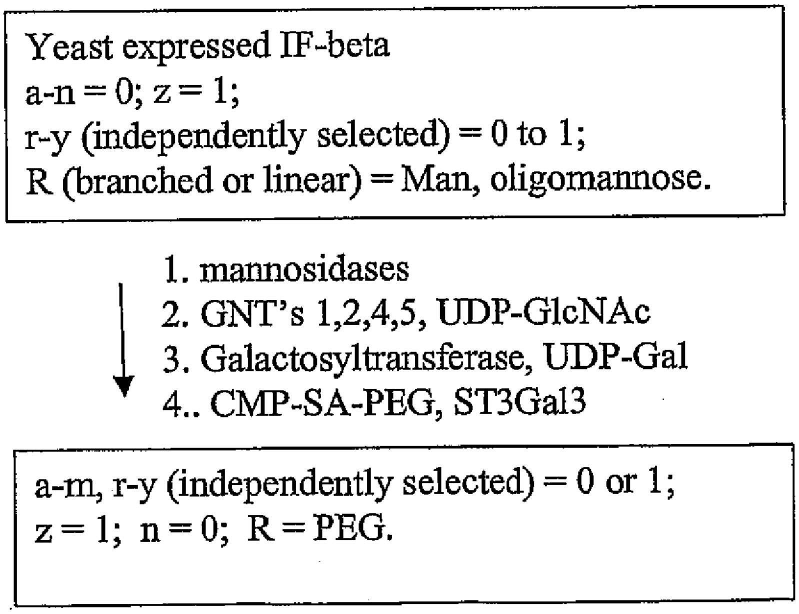
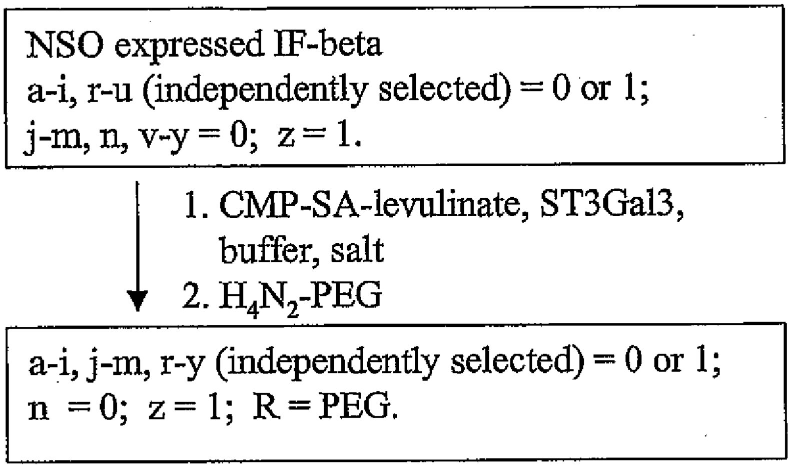

Yeast expressed IF-beta
a-n = 0; z = 1;
r-y (independently selected) = 0 to 1;
R (branched or linear) = Man, oligomannose.
1. mannosidases
2. GNT's 1,2,4,5, UDP-GlcNAc
3. Galactosyltransferase, UDP-Gal
4.. CMP-SA-PEG, ST3Gal3
a-m, r-y (independently selected) = 0 or 1;
z = 1; n = 0; R = PEG.

FIG. 29G

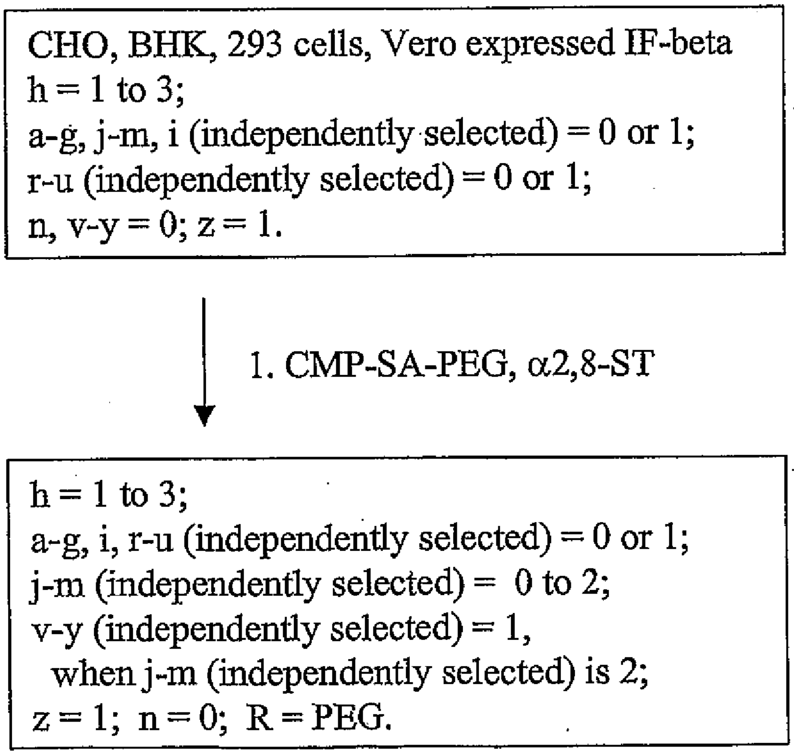


NSO expressed IF-beta
a-i, r-u (independently selected) = 0 or 1;
j-m, n, v-y = 0; z = 1.

1. CMP-SA-levulinate, ST3Gal3, buffer, salt
2. H_4N_2-PEG

a-i, j-m, r-y (independently selected) = 0 or 1;
n = 0; z = 1; R = PEG.

FIG. 29H



CHO, BHK, 293 cells, Vero expressed IF-beta
h = 1 to 3;
a-g, j-m, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
n, v-y = 0; z = 1.

1. CMP-SA-PEG, α2,8-ST

h = 1 to 3;
a-g, i, r-u (independently selected) = 0 or 1;
j-m (independently selected) = 0 to 2;
v-y (independently selected) = 1,
when j-m (independently selected) is 2;
z = 1; n = 0; R = PEG.

FIG. 29I

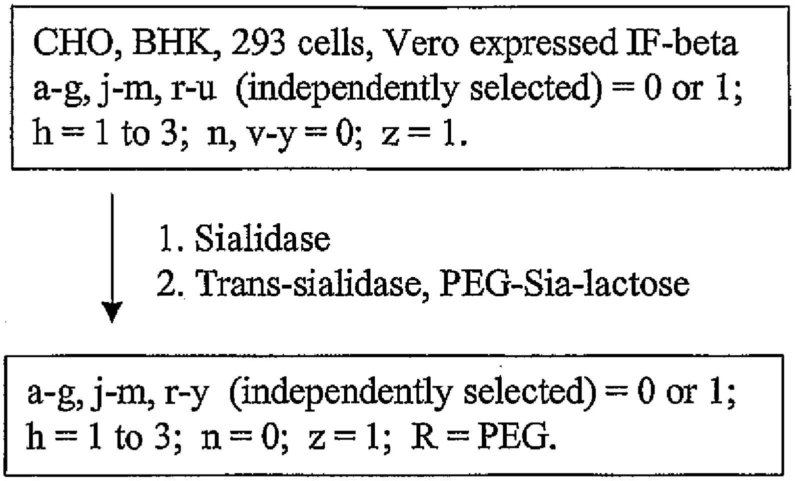

CHO, BHK, 293 cells, Vero expressed IF-beta
a-g, j-m, r-u (independently selected) = 0 or 1;
h = 1 to 3; n, v-y = 0; z = 1.
1. Sialidase
2. Trans-sialidase, PEG-Sia-lactose
a-g, j-m, r-y (independently selected) = 0 or 1;
h = 1 to 3; n = 0; z = 1; R = PEG.

FIG. 29J

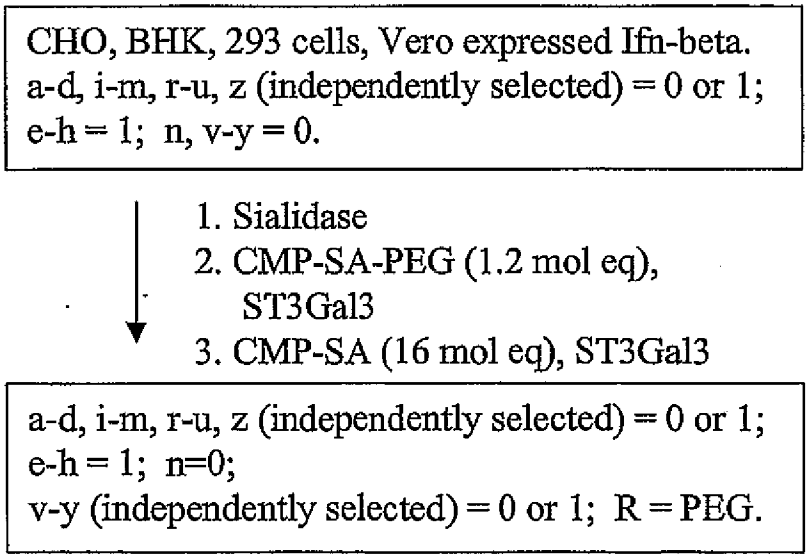

CHO, BHK, 293 cells, Vero expressed Ifn-beta.
a-d, i-m, r-u, z (independently selected) = 0 or 1;
e-h = 1; n, v-y = 0.
1. Sialidase
2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
3. CMP-SA (16 mol eq), ST3Gal3
a-d, i-m, r-u, z (independently selected) = 0 or 1;
e-h = 1; n=0;
v-y (independently selected) = 0 or 1; R = PEG.

FIG. 29K

NSO expressed Ifn-beta.
a-d, i-m, r-u, z (independently selected) = 0 or 1;
e-h = 1; n, v-y = 0;
Sia (independently selected) = Sia or Gal.

1. Sialidase and α-galactosidase
2. α-Galactosyltransferase, UDP-Gal
3. CMP-SA-PEG, ST3Gal3

a-d, i-m, r-u, z (independently selected) = 0 or 1;
e-h = 1; R = PEG
n = 0; v-y (independently selected) = 1,
when j-m (independently selected) is 1;

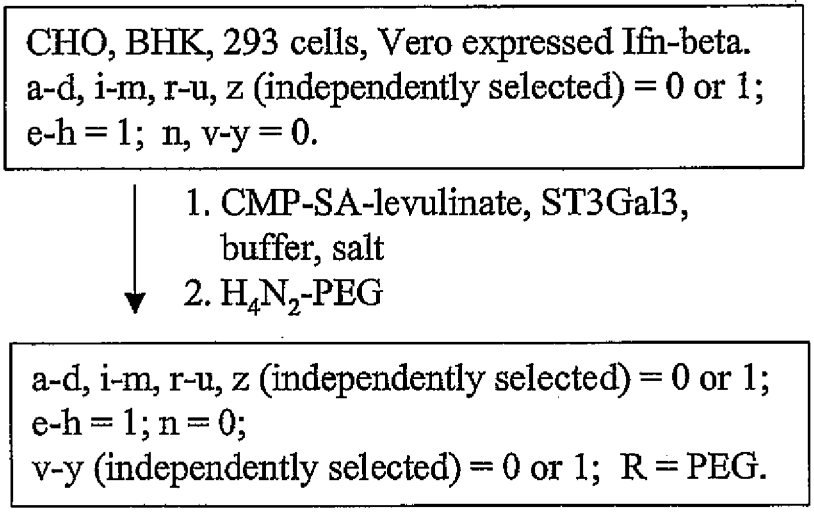
FIG. 29L

CHO, BHK, 293 cells, Vero expressed Ifn-beta.
a-d, i-m, r-u, z (independently selected) = 0 or 1;
e-h = 1; n, v-y = 0.

1. Sialidase
2. CMP-SA-PEG (16 mol eq), ST3Gal3
3. CMP-SA, ST3Gal3

a-d, i-m, r-u, z (independently selected) = 0 or 1;
e-h = 1; n = 0;
v-y (independently selected) = 0 or 1; R = PEG.

FIG. 29M

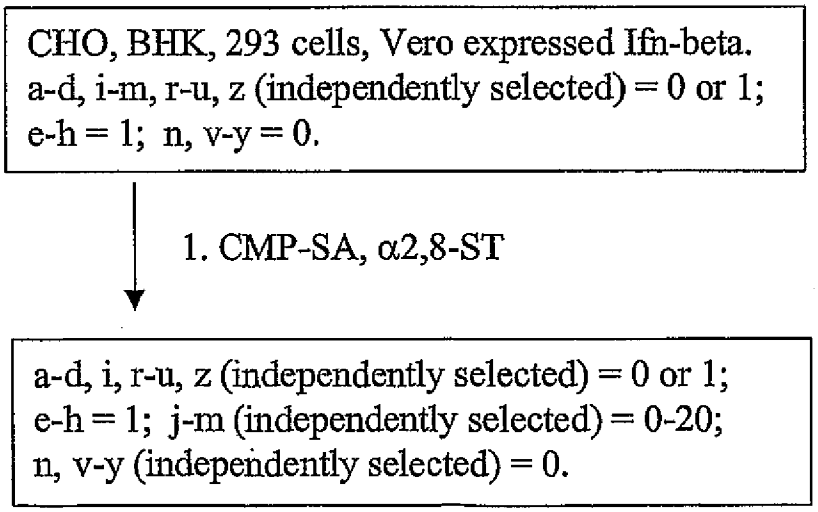


CHO, BHK, 293 cells, Vero expressed Ifn-beta.
a-d, i-m, r-u, z (independently selected) = 0 or 1;
e-h = 1; n, v-y = 0.

1. CMP-SA-levulinate, ST3Gal3, buffer, salt
2. H_4N_2-PEG

a-d, i-m, r-u, z (independently selected) = 0 or 1;
e-h = 1; n = 0;
v-y (independently selected) = 0 or 1; R = PEG.

FIG. 29N

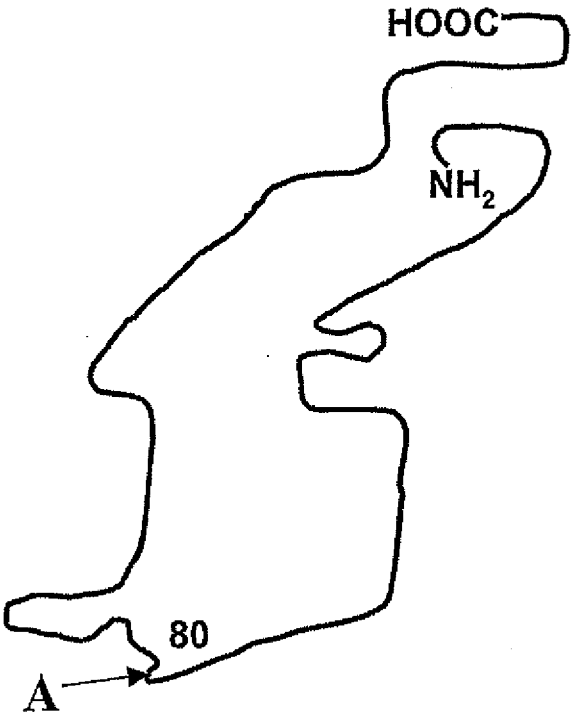


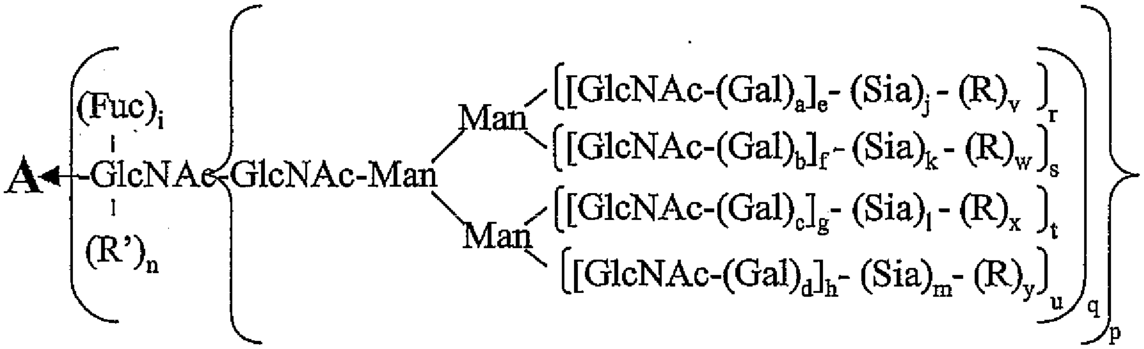
CHO, BHK, 293 cells, Vero expressed Ifn-beta.
a-d, i-m, r-u, z (independently selected) = 0 or 1;
e-h = 1; n, v-y = 0.

1. CMP-SA, α2,8-ST

a-d, i, r-u, z (independently selected) = 0 or 1;
e-h = 1; j-m (independently selected) = 0-20;
n, v-y (independently selected) = 0.

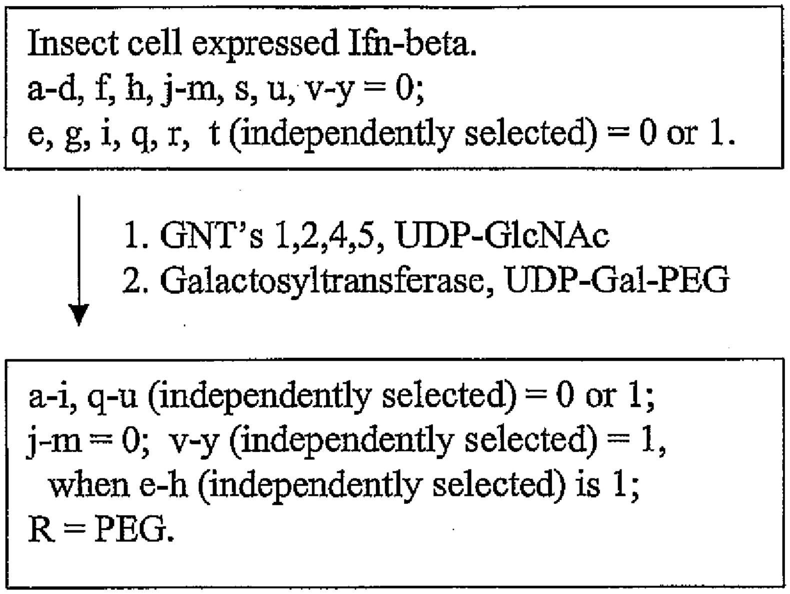
FIG. 29O




A
(Fuc)$_i$
GlcNAc
(R')$_n$
GlcNAc-Man
Man
Man
[[GlcNAc-(Gal)$_a$]$_e$- (Sia)$_j$ - (R)$_v$]$_r$
[[GlcNAc-(Gal)$_b$]$_f$- (Sia)$_k$ - (R)$_w$]$_s$
[[GlcNAc-(Gal)$_c$]$_g$- (Sia)$_l$ - (R)$_x$]$_t$
[[GlcNAc-(Gal)$_d$]$_h$- (Sia)$_m$- (R)$_y$]$_u$
q
p

a-d, i, p-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0; R = modifying group;
R' = H, glycosyl group, modifying group, glycoconjugate.

FIG. 29P

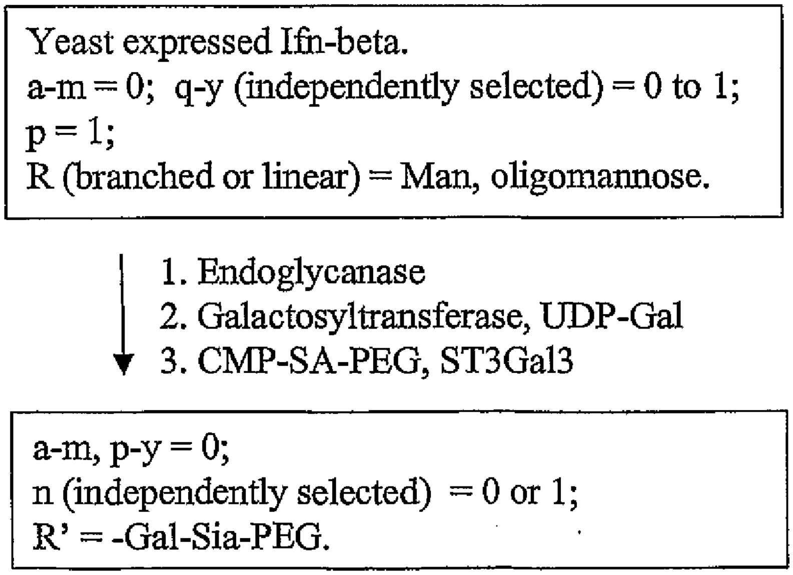


Insect cell expressed Ifn-beta.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.

1. GNT's 1,2,4,5, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal-PEG

a-i, q-u (independently selected) = 0 or 1;
j-m = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.

FIG. 29Q

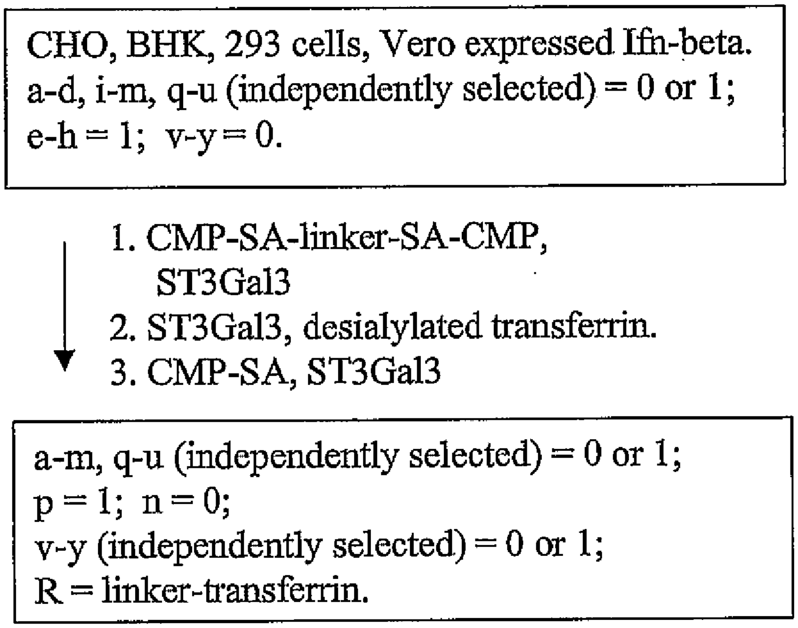


Yeast expressed Ifn-beta.
a-m = 0; q-y (independently selected) = 0 to 1;
p = 1;
R (branched or linear) = Man, oligomannose.

1. Endoglycanase
2. Galactosyltransferase, UDP-Gal
3. CMP-SA-PEG, ST3Gal3

a-m, p-y = 0;
n (independently selected) = 0 or 1;
R' = -Gal-Sia-PEG.

FIG. 29R

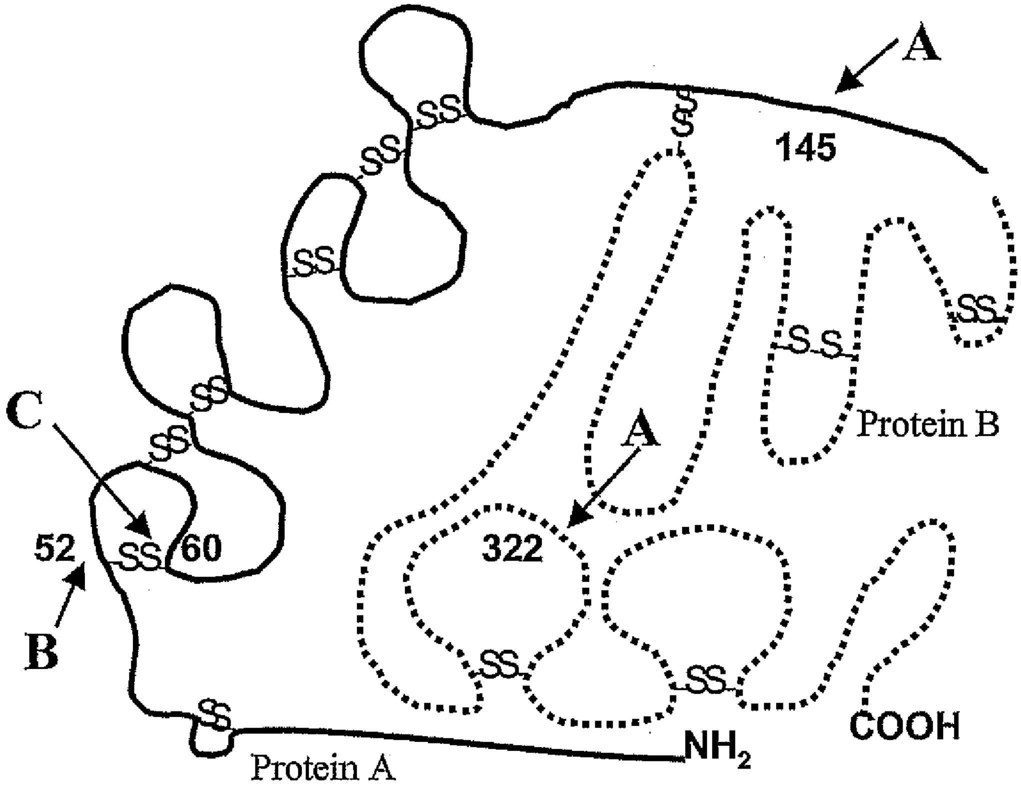


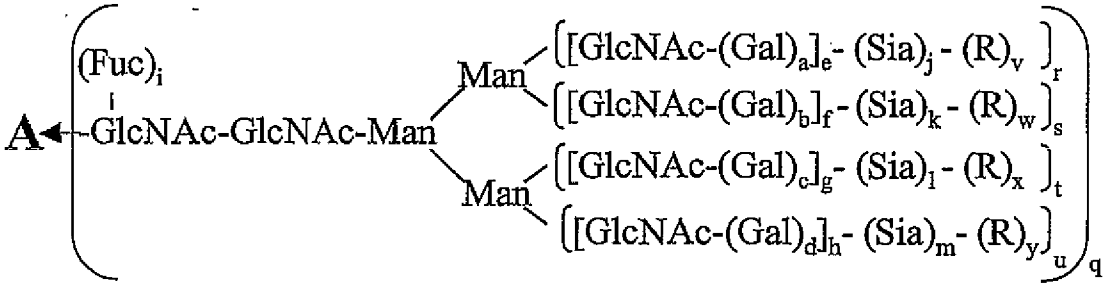
CHO, BHK, 293 cells, Vero expressed Ifn-beta.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. CMP-SA-linker-SA-CMP, ST3Gal3
2. ST3Gal3, desialylated transferrin.
3. CMP-SA, ST3Gal3

a-m, q-u (independently selected) = 0 or 1;
p = 1; n = 0;
v-y (independently selected) = 0 or 1;
R = linker-transferrin.

FIG. 29S





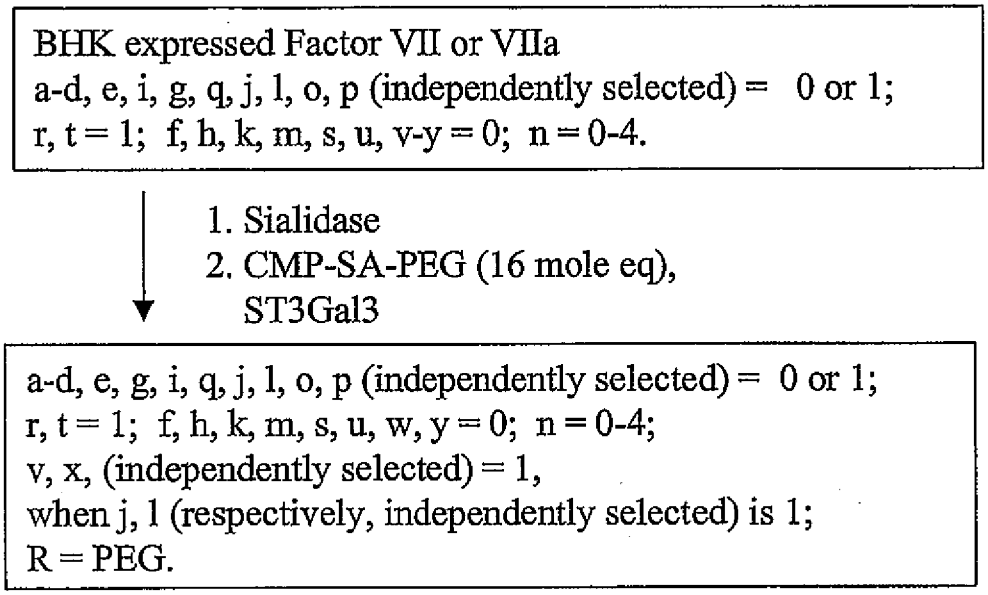
$$A \leftarrow \left(\begin{array}{l} (Fuc)_i \\ | \\ \text{-GlcNAc-GlcNAc-Man} \begin{array}{l} \text{Man} \begin{array}{l} \left([\text{GlcNAc-(Gal)}_a]_e\text{- (Sia)}_j\text{ - (R)}_v\right]_r \\ \left([\text{GlcNAc-(Gal)}_b]_f\text{- (Sia)}_k\text{ - (R)}_w\right]_s \end{array} \\ \text{Man} \begin{array}{l} \left([\text{GlcNAc-(Gal)}_c]_g\text{- (Sia)}_l\text{ - (R)}_x\right]_t \\ \left([\text{GlcNAc-(Gal)}_d]_h\text{- (Sia)}_m\text{ - (R)}_y\right]_u \end{array} \end{array} \end{array} \right)_q$$

$B \leftarrow \left[\text{Glc-(Xyl)}_n\right]_o$

$C \leftarrow \left[\text{-Fuc}\right]_p$

a-d, i, q-u (independently selected) = 0 or 1.
o, p (independently selected) = 0 or 1.
e-h, n (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 20.
v-y = 0;
R = modifying group, mannose, oligomannose, Sia-Lewis X, Sia-Lewis A..

FIG. 30A

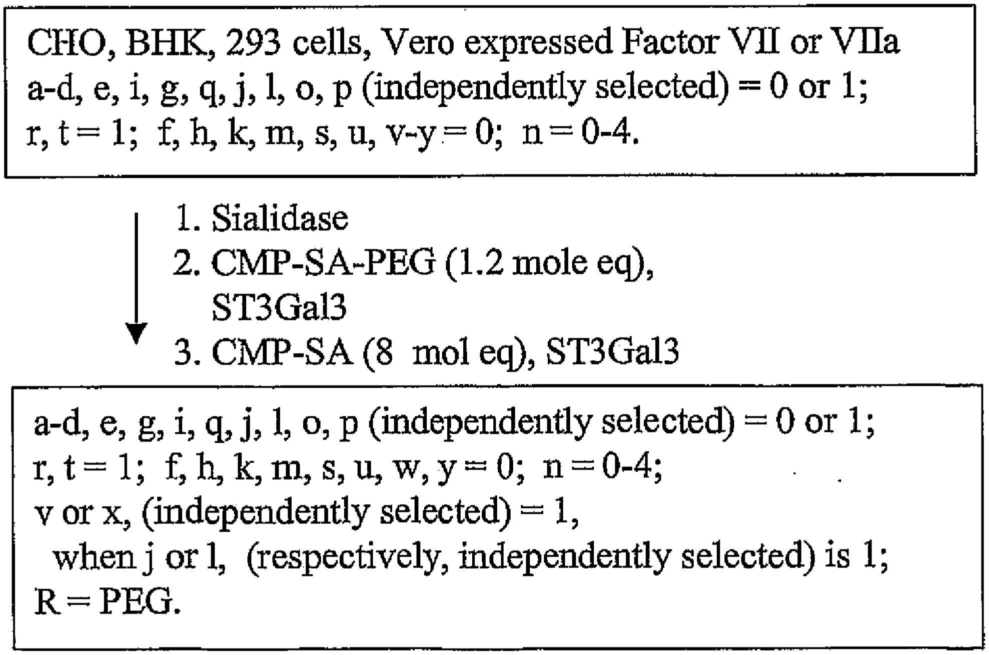


BHK expressed Factor VII or VIIa
a-d, e, i, g, q, j, l, o, p (independently selected) = 0 or 1;
r, t = 1; f, h, k, m, s, u, v-y = 0; n = 0-4.

1. Sialidase
2. CMP-SA-PEG (16 mole eq), ST3Gal3

a-d, e, g, i, q, j, l, o, p (independently selected) = 0 or 1;
r, t = 1; f, h, k, m, s, u, w, y = 0; n = 0-4;
v, x, (independently selected) = 1,
when j, l (respectively, independently selected) is 1;
R = PEG.

FIG. 30B



CHO, BHK, 293 cells, Vero expressed Factor VII or VIIa
a-d, e, i, g, q, j, l, o, p (independently selected) = 0 or 1;
r, t = 1; f, h, k, m, s, u, v-y = 0; n = 0-4.

1. Sialidase
2. CMP-SA-PEG (1.2 mole eq), ST3Gal3
3. CMP-SA (8 mol eq), ST3Gal3

a-d, e, g, i, q, j, l, o, p (independently selected) = 0 or 1;
r, t = 1; f, h, k, m, s, u, w, y = 0; n = 0-4;
v or x, (independently selected) = 1,
when j or l, (respectively, independently selected) is 1;
R = PEG.

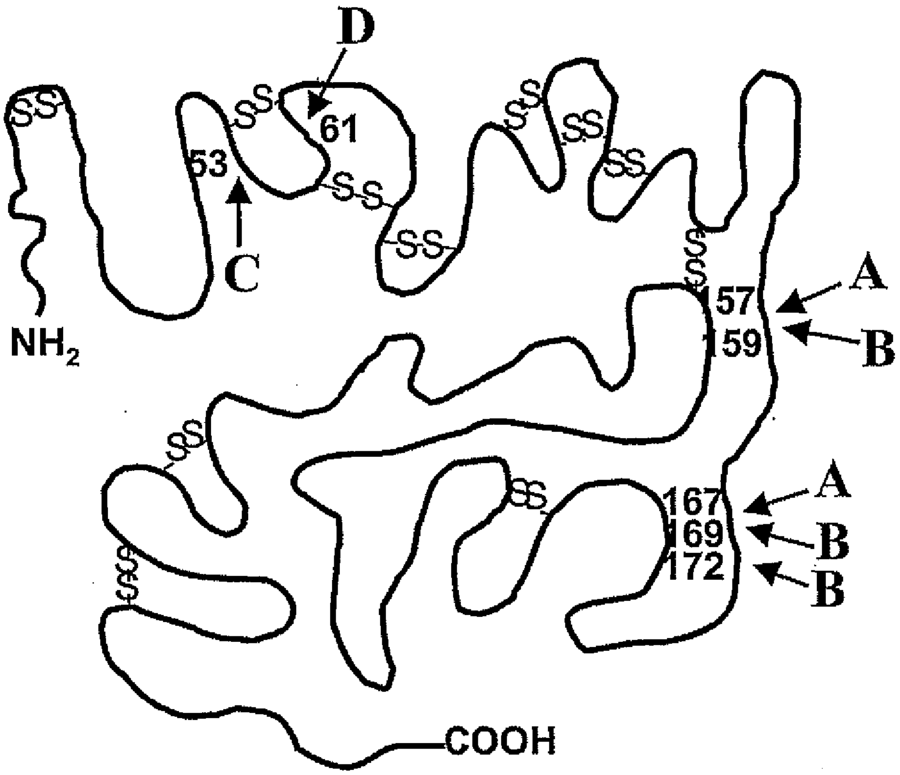
FIG. 30C

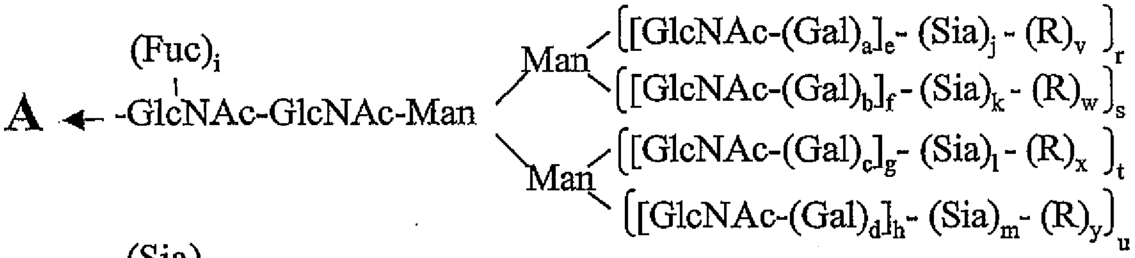
NSO expressed Factor VII or VIIa
a--u (independently selected) = 0 or 1;
v-y = 0; n = 0-4;
Sia (independently selected) = Sia or Gal.

1. Sialidase and α-galactosidase
2. Galactosyltransferase, UDP-Gal
3. CMP-SA-PEG, ST3Gal3

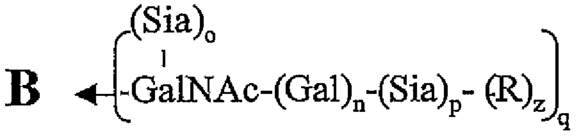
a-m, o-u (independently selected) = 0 or 1;
n = 0-4; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
Sia = Sia; R = PEG.

FIG. 30D





$$\mathbf{A} \leftarrow \overset{(\mathrm{Fuc})_i}{\text{-GlcNAc}}\text{-GlcNAc-Man}\begin{cases}\text{Man}\begin{cases}\left[[\mathrm{GlcNAc}\text{-}(\mathrm{Gal})_a]_e\text{-}(\mathrm{Sia})_j\text{-}(\mathrm{R})_v\right]_r\\ \left[[\mathrm{GlcNAc}\text{-}(\mathrm{Gal})_b]_f\text{-}(\mathrm{Sia})_k\text{-}(\mathrm{R})_w\right]_s\end{cases}\\ \text{Man}\begin{cases}\left[[\mathrm{GlcNAc}\text{-}(\mathrm{Gal})_c]_g\text{-}(\mathrm{Sia})_l\text{-}(\mathrm{R})_x\right]_t\\ \left[[\mathrm{GlcNAc}\text{-}(\mathrm{Gal})_d]_h\text{-}(\mathrm{Sia})_m\text{-}(\mathrm{R})_y\right]_u\end{cases}\end{cases}$$



$$\mathbf{B} \leftarrow \left[\overset{(\mathrm{Sia})_o}{\text{-GalNAc}}\text{-}(\mathrm{Gal})_n\text{-}(\mathrm{Sia})_p\text{-}(\mathrm{R})_z\right]_q$$

$$\mathbf{C} \leftarrow \left[\text{-Glc-}(\mathrm{Xyl})_{aa}\right]_{bb}$$

$$\mathbf{D} \leftarrow \text{-Fuc}\left[\text{-}(\mathrm{GlcNAc})_{cc}\text{-}(\mathrm{Gal})_{dd}\text{-}(\mathrm{Sia})_{ee}\right]_{ff}\text{-}(\mathrm{R})_{gg}$$

a-d, i, n-u (independently selected) = 0 or 1.
bb, cc, dd, ee, ff, gg (independently selected) = 0 or 1.
e-h, aa (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 20.
v-z = 0; R = modifying group, mannose, oligo-mannose.

FIG. 31A

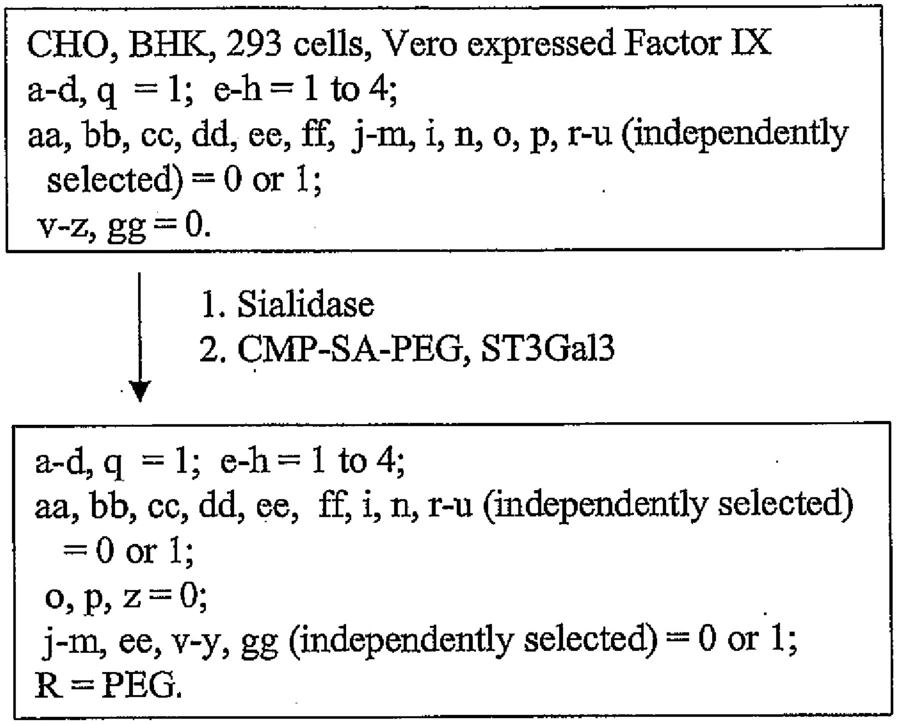

CHO, BHK, 293 cells, Vero expressed Factor IX
a-d, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, j-m, i, n, o, p, r-u (independently selected) = 0 or 1;
v-z, gg = 0.
1. Sialidase
2. CMP-SA-PEG, ST3Gal3
a-d, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, i, n, r-u (independently selected) = 0 or 1;
o, p, z = 0;
j-m, ee, v-y, gg (independently selected) = 0 or 1;
R = PEG.

FIG. 31B

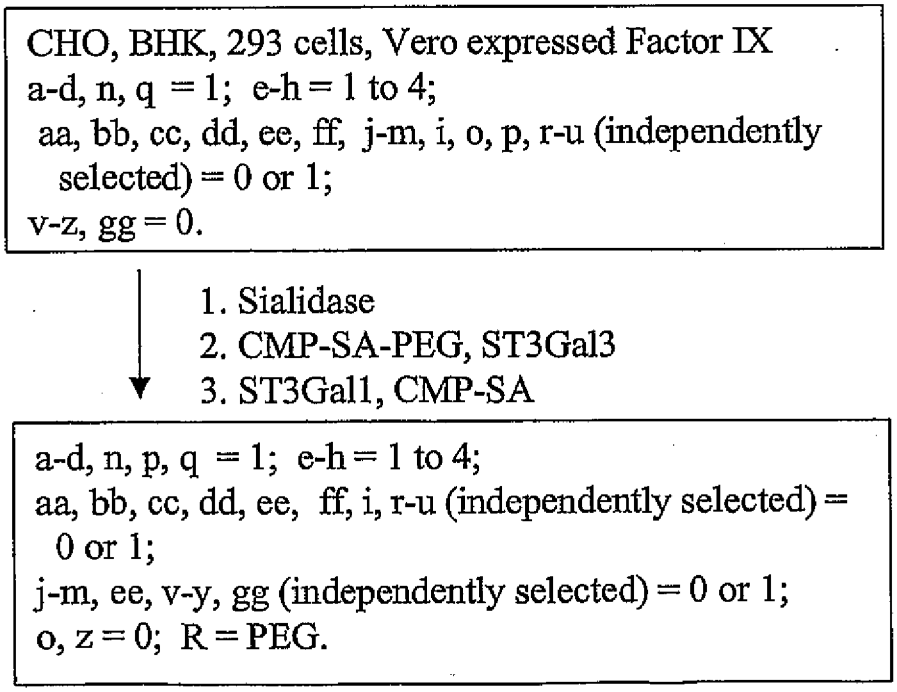

CHO, BHK, 293 cells, Vero expressed Factor IX
a-d, n, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, j-m, i, o, p, r-u (independently selected) = 0 or 1;
v-z, gg = 0.
1. Sialidase
2. CMP-SA-PEG, ST3Gal3
3. ST3Gal1, CMP-SA
a-d, n, p, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, i, r-u (independently selected) = 0 or 1;
j-m, ee, v-y, gg (independently selected) = 0 or 1;
o, z = 0; R = PEG.

FIG. 31C

CHO, BHK, 293 cells, Vero expressed Factor IX
a-d, n, q, bb, cc, dd, ff = 1; e-h, aa = 1 to 4; ee, j-m, i, o, p, r-u (independently selected) = 0 or 1; v-z, gg = 0.

↓

1. sialidase
2. Galactosyltransferase, UDP-Gal
3. CMP-SA, ST3Gal3
4. CMP-SA-PEG, ST3Gal1

a-d, n, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, i, r-u (independently selected) = 0 or 1; R = PEG;
o, v-y, gg = 0;
j-m, p, ee (independently selected) = 0 or 1, but when p = 1, z = 1.

FIG. 31D

CHO, BHK, 293 cells, Vero expressed Factor IX
a-d, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, j-m, i, n, o, p, r-u (independently selected) = 0 or 1;
v-z, gg = 0.

↓ CMP-SA-PEG, ST3Gal3

a-d, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, i, n, r-u (independently selected) = 0 or 1; R = PEG;
o, p, z = 0; j-m, ee, v-y, gg (independently selected) = 0 or 1.

FIG. 31E

CHO, BHK, 293 cells, Vero expressed Factor IX
a-d, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, j-m, i, n, o, p, r-u (independently selected) = 0 or 1;
v-z, gg = 0.

1. CMP-SA-levulinate, ST3Gal3, buffer, salt
2. H_4N_2-PEG

a-d, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, i, n, r-u (independently selected) = 0 or 1;
o, p, z = 0; R = PEG;
j-m, ee, v-y, gg (independently selected) = 0 or 1.

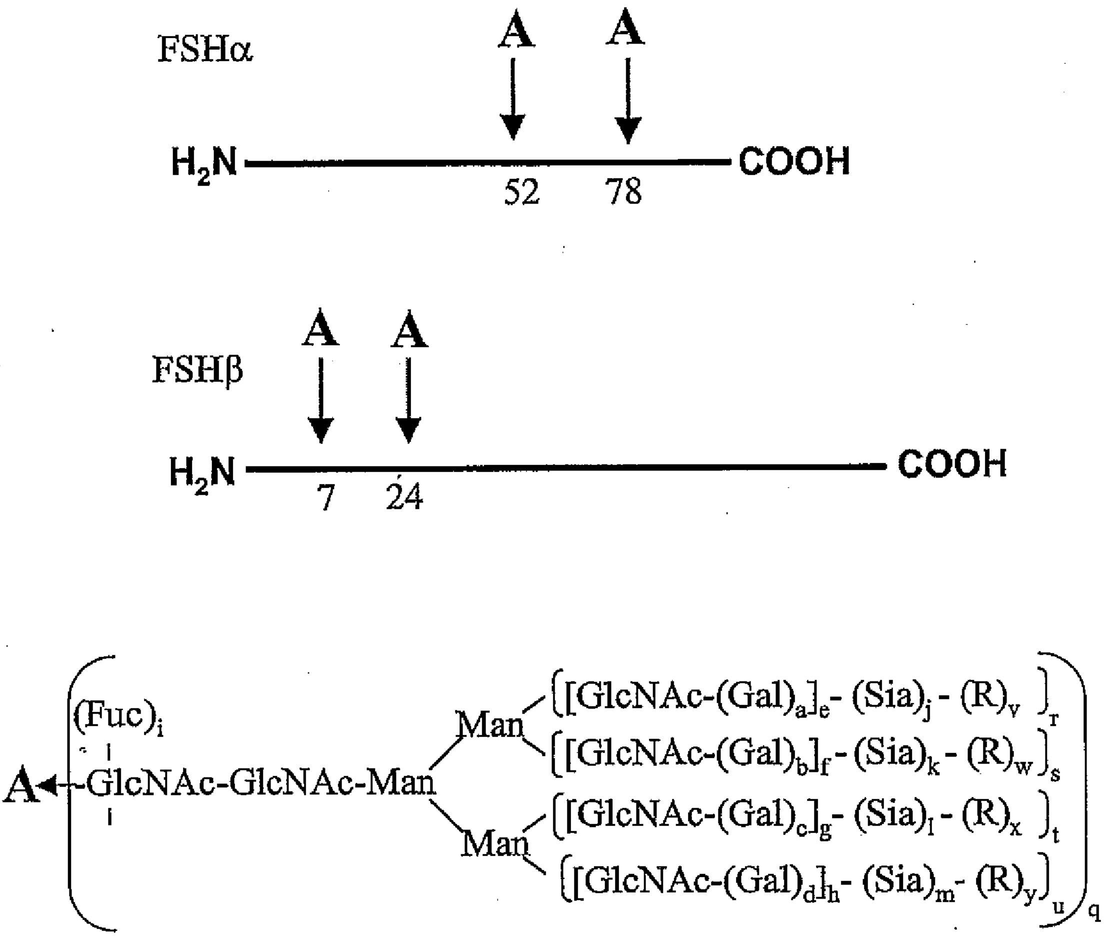
FIG. 31F

CHO, BHK, 293 cells, Vero expressed Factor IX
a-d, n, q, bb, cc, dd, ff = 1;
e-h, aa = 1 to 4;
ee, j-m, i, o, p, r-u (independently selected) = 0 or 1;
v-z, gg = 0.

1. CMP-SA-PEG, α2,8-ST

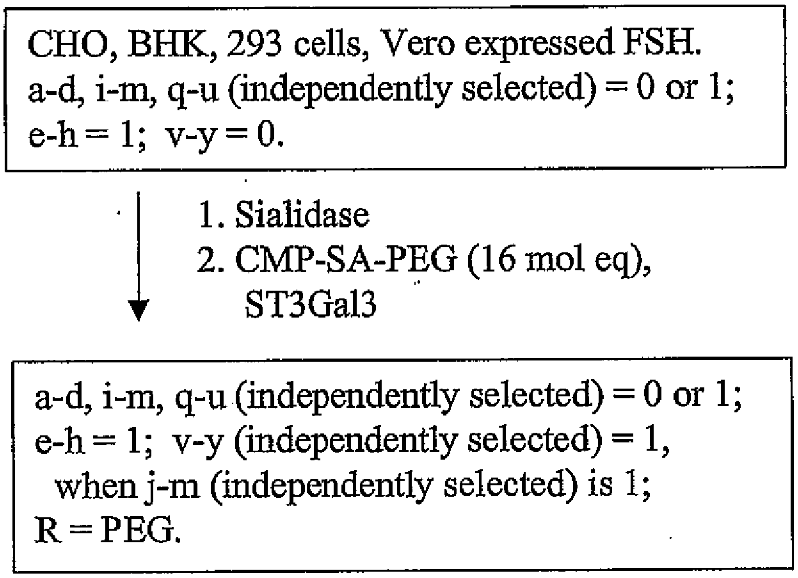
a-d, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, i, n, r-u (independently selected) = 0 or 1;
o, p, z = 0; R= PEG;
j-m, ee (independently selected) = 0 to 2;
v-y, gg (independently selected) = 1, when j-m (independently selected) is 2;

FIG. 31G


FSHα
A
A
H2N
COOH
52
78
FSHβ
A
A
H2N
COOH
7
24
(Fuc)i
A
GlcNAc-GlcNAc-Man
Man
Man
[GlcNAc-(Gal)a]e- (Sia)j - (R)v r
[GlcNAc-(Gal)b]f- (Sia)k - (R)w s
[GlcNAc-(Gal)c]g- (Sia)l - (R)x t
[GlcNAc-(Gal)d]h- (Sia)m- (R)y u
q

a-d, i, q-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0;
R = modifying group, mannose, oligo-mannose.

FIG. 32A

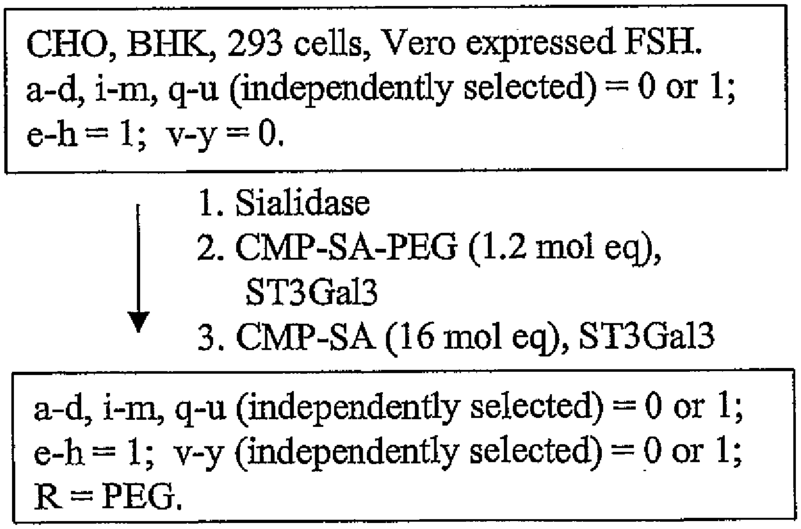


CHO, BHK, 293 cells, Vero expressed FSH.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. Sialidase
2. CMP-SA-PEG (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1, when j-m (independently selected) is 1;
R = PEG.

FIG. 32B



CHO, BHK, 293 cells, Vero expressed FSH.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. Sialidase
2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
3. CMP-SA (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 32C

NSO expressed FSH.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0;
Sia (independently selected) = Sia or Gal.

1. Sialidase and α-galactosidase
2. Galactosyltransferase, UDP-Gal
3. CMP-SA-PEG, ST3Gal1

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.

FIG. 32D

CHO, BHK, 293 cells, Vero expressed FSH.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. Sialidase
2. CMP-SA-PEG (16 mol eq), ST3Gal3
3. CMP-SA, ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 32E

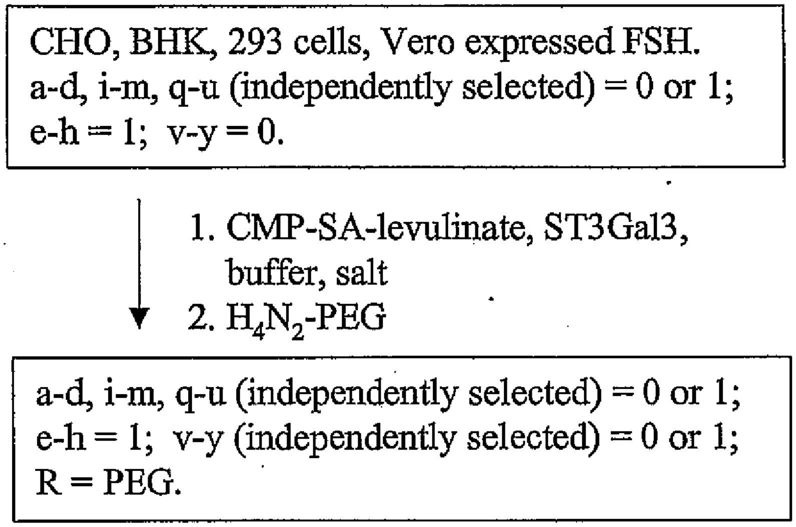

CHO, BHK, 293 cells, Vero expressed FSH.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
1. CMP-SA-levulinate, ST3Gal3, buffer, salt
2. H_4N_2-PEG
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 32F

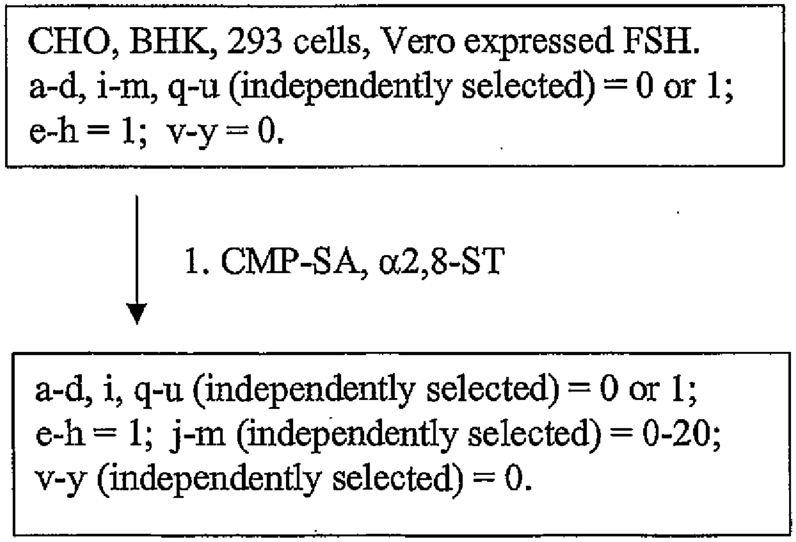

CHO, BHK, 293 cells, Vero expressed FSH.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
1. CMP-SA, α2,8-ST
a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1; j-m (independently selected) = 0-20;
v-y (independently selected) = 0.

FIG. 32G

Insect cell expressed FSH.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.

↓
1. GNT's 1,2,4,5, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal-PEG

a-i, q-u (independently selected) = 0 or 1;
j-m = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.

FIG. 32H

Yeast expressed FSH.
a-m = 0; q-y (independently selected) = 0 to 1;
p = 1;
R (branched or linear) = Man, oligomannose.

↓
1. Endoglycanase
2. Galactosyltransferase, UDP-Gal
3. CMP-SA-PEG, ST3Gal3

a-m, p-y = 0;
n (independently selected) = 0 or 1;
R' = -Gal-Sia-PEG.

FIG. 32I

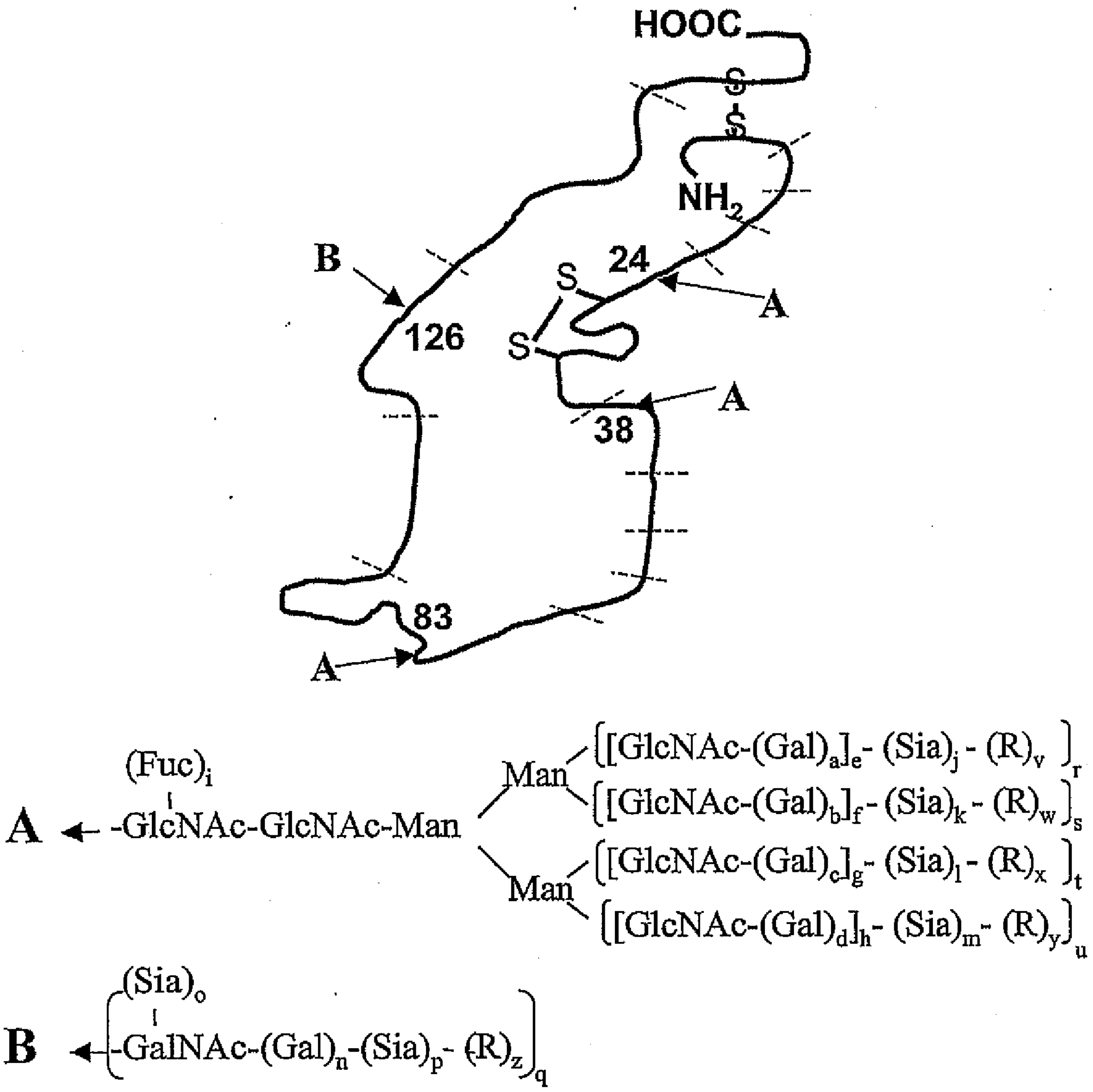
CHO, BHK, 293 cells, Vero expressed FSH.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

↓

1. CMP-SA-linker-SA-CMP, ST3Gal3
2. ST3Gal1, desialylated chorionic gonadrophin (CG) produced in CHO.
3. CMP-SA, ST3Gal3, ST3Gal1

a-m, q-u (independently selected) = 0 or 1;
p = 1; n = 0;
v-y (independently selected) = 0 or 1;
R = linker-CG.

FIG. 32J



$$\mathbf{A} \leftarrow \text{-}\overset{(\mathrm{Fuc})_i}{\mathrm{GlcNAc}}\text{-GlcNAc-Man}\begin{cases}\mathrm{Man}\begin{cases}\{[\text{GlcNAc-(Gal)}_a]_e\text{-}(\mathrm{Sia})_j\text{-}(\mathrm{R})_v\}_r\\ \{[\text{GlcNAc-(Gal)}_b]_f\text{-}(\mathrm{Sia})_k\text{-}(\mathrm{R})_w\}_s\end{cases}\\ \mathrm{Man}\begin{cases}\{[\text{GlcNAc-(Gal)}_c]_g\text{-}(\mathrm{Sia})_l\text{-}(\mathrm{R})_x\}_t\\ \{[\text{GlcNAc-(Gal)}_d]_h\text{-}(\mathrm{Sia})_m\text{-}(\mathrm{R})_y\}_u\end{cases}\end{cases}$$

$$\mathbf{B} \leftarrow \left\{\text{-}\overset{(\mathrm{Sia})_o}{\mathrm{GalNAc}}\text{-}(\mathrm{Gal})_n\text{-}(\mathrm{Sia})_p\text{-}(\mathrm{R})_z\right\}_q$$

a-d, i, n-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
j-m (independently selected) = 0 to 20.
v-z = 0;
R = modifying group, mannose, oligo-mannose.

FIG. 33A

CHO, BHK, 293 cells, Vero expressed EPO
a-g, n, q = 1; h = 1 to 3;
j-m, i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 to1; v-z = 0

↓
1. Sialidase
2. CMP-SA-PEG, ST3Gal3

a-g, n, q = 1; h = 1 to 3;
i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
j-m, v-y (independently selected) = 0 or 1;
R = PEG; z = 0.

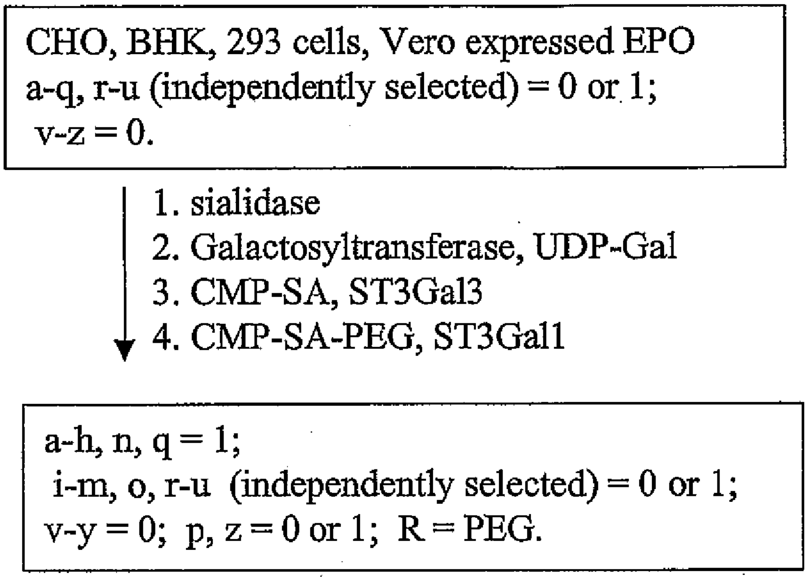
FIG. 33B

Insect cell expressed EPO
a-d, f, h, j-q, s, u, v-z = 0;
e, g, i, r, t (independently selected) = 0 or 1.

↓
1. GNT's 1&2, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal
2. CMP-SA-PEG, ST3Gal3

b, d, f, h, k, m-q, s, u, w, y, z = 0;
a, c, e, g, i, r, t (independently selected)= 0 or 1;
j, l, v, x (independently selected) = 0 or 1;
R = PEG.

FIG. 33C

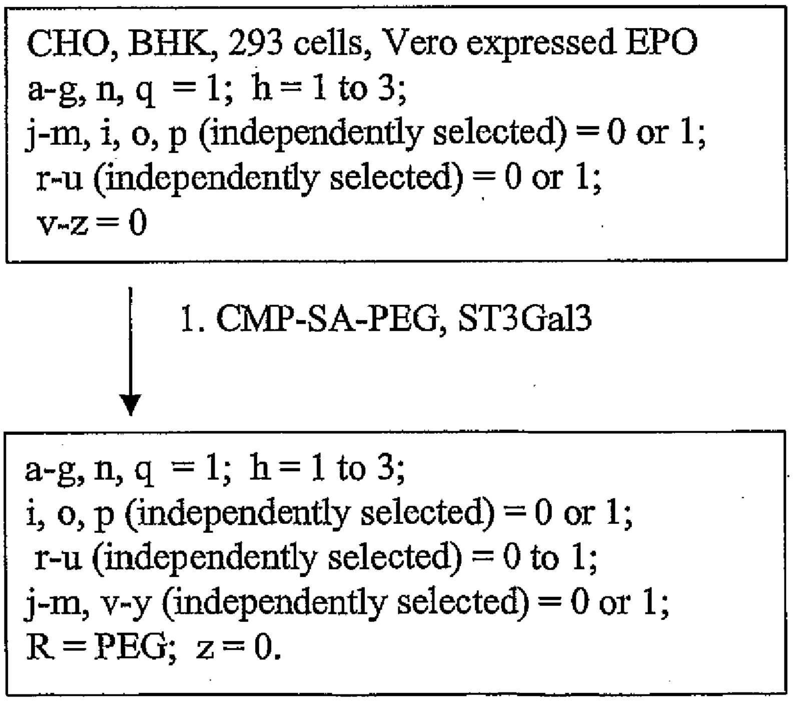


CHO, BHK, 293 cells, Vero expressed EPO
a-q, r-u (independently selected) = 0 or 1;
v-z = 0.

1. sialidase
2. Galactosyltransferase, UDP-Gal
3. CMP-SA, ST3Gal3
4. CMP-SA-PEG, ST3Gal1

a-h, n, q = 1;
i-m, o, r-u (independently selected) = 0 or 1;
v-y = 0; p, z = 0 or 1; R = PEG.

FIG. 33D



CHO, BHK, 293 cells, Vero expressed EPO
a-g, n, q = 1; h = 1 to 3;
j-m, i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
v-z = 0

1. CMP-SA-PEG, ST3Gal3

a-g, n, q = 1; h = 1 to 3;
i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 to 1;
j-m, v-y (independently selected) = 0 or 1;
R = PEG; z = 0.

FIG. 33E

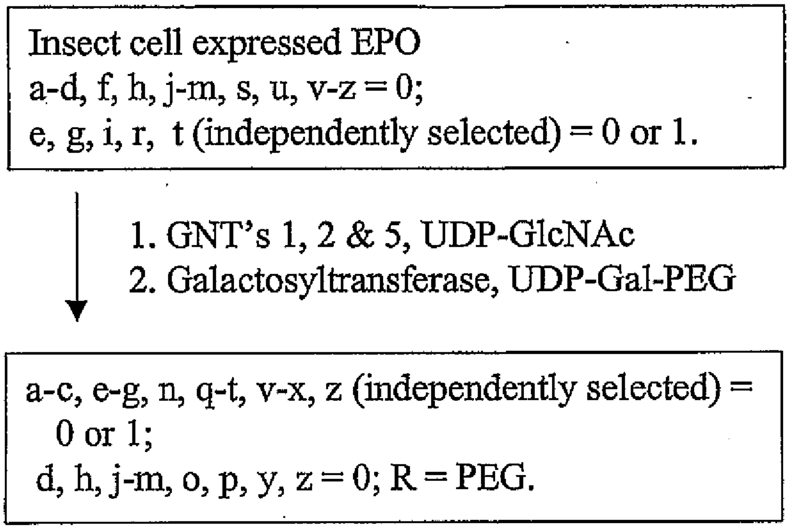

Insect cell expressed EPO
a-d, f, h, j-m, s, u, v-z = 0;
e, g, i, r, t (independently selected) = 0 or 1.
1. GNT's 1, 2 & 5, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal-PEG
a-c, e-g, n, q-t, v-x, z (independently selected) = 0 or 1;
d, h, j-m, o, p, y, z = 0; R = PEG.

FIG. 33F

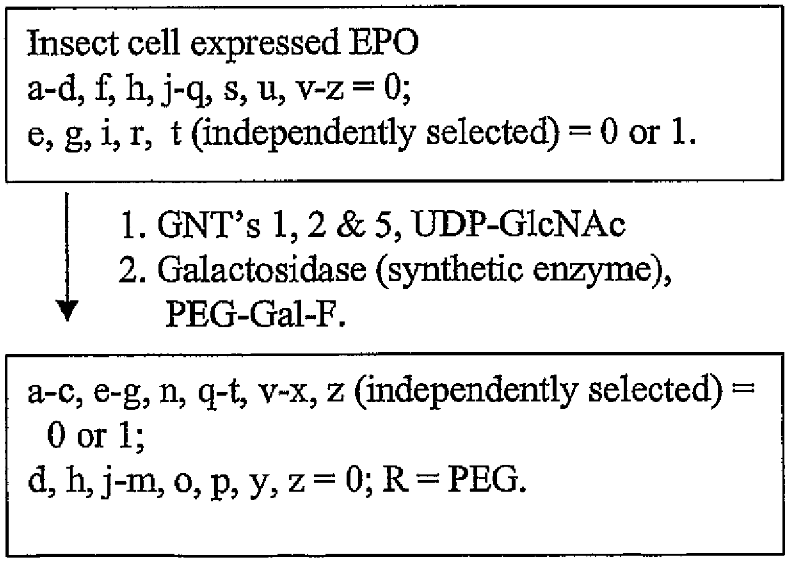
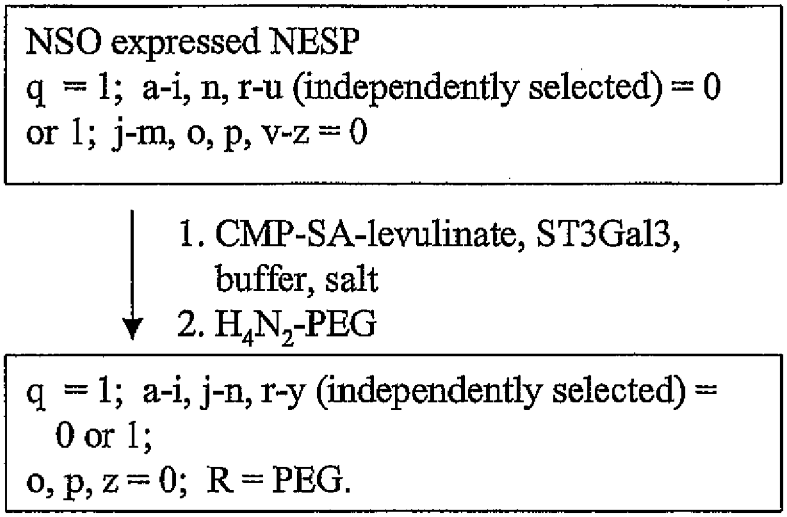

Insect cell expressed EPO
a-d, f, h, j-q, s, u, v-z = 0;
e, g, i, r, t (independently selected) = 0 or 1.
1. GNT's 1, 2 & 5, UDP-GlcNAc
2. Galactosidase (synthetic enzyme), PEG-Gal-F.
a-c, e-g, n, q-t, v-x, z (independently selected) = 0 or 1;
d, h, j-m, o, p, y, z = 0; R = PEG.

FIG. 33G

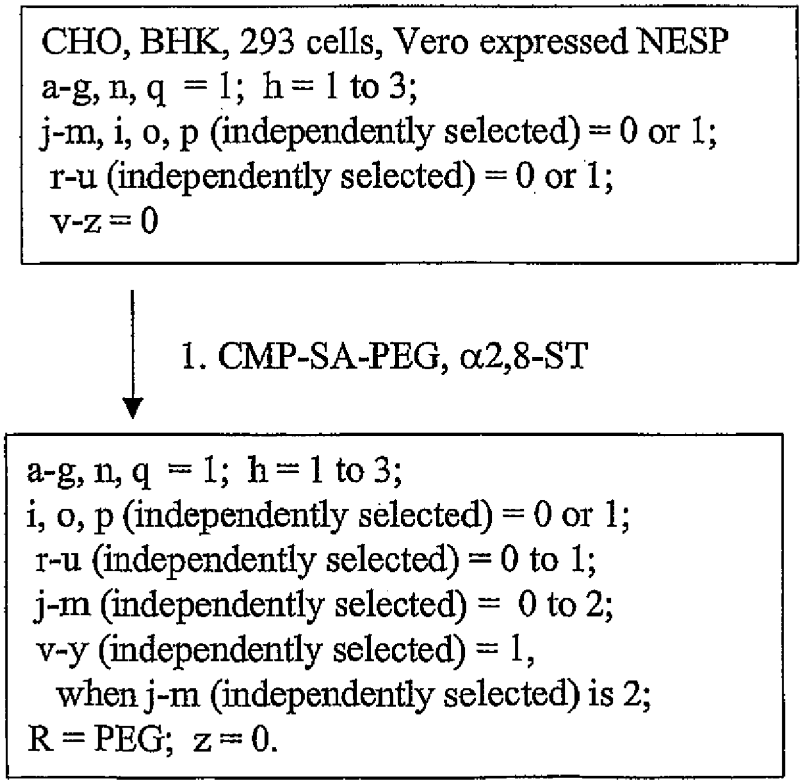


NSO expressed NESP
q = 1; a-i, n, r-u (independently selected) = 0 or 1; j-m, o, p, v-z = 0

1. CMP-SA-levulinate, ST3Gal3, buffer, salt
2. H_4N_2-PEG

q = 1; a-i, j-n, r-y (independently selected) = 0 or 1;
o, p, z = 0; R = PEG.

FIG. 33H



CHO, BHK, 293 cells, Vero expressed NESP
a-g, n, q = 1; h = 1 to 3;
j-m, i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
v-z = 0

1. CMP-SA-PEG, α2,8-ST

a-g, n, q = 1; h = 1 to 3;
i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 to 1;
j-m (independently selected) = 0 to 2;
v-y (independently selected) = 1, when j-m (independently selected) is 2;
R = PEG; z = 0.

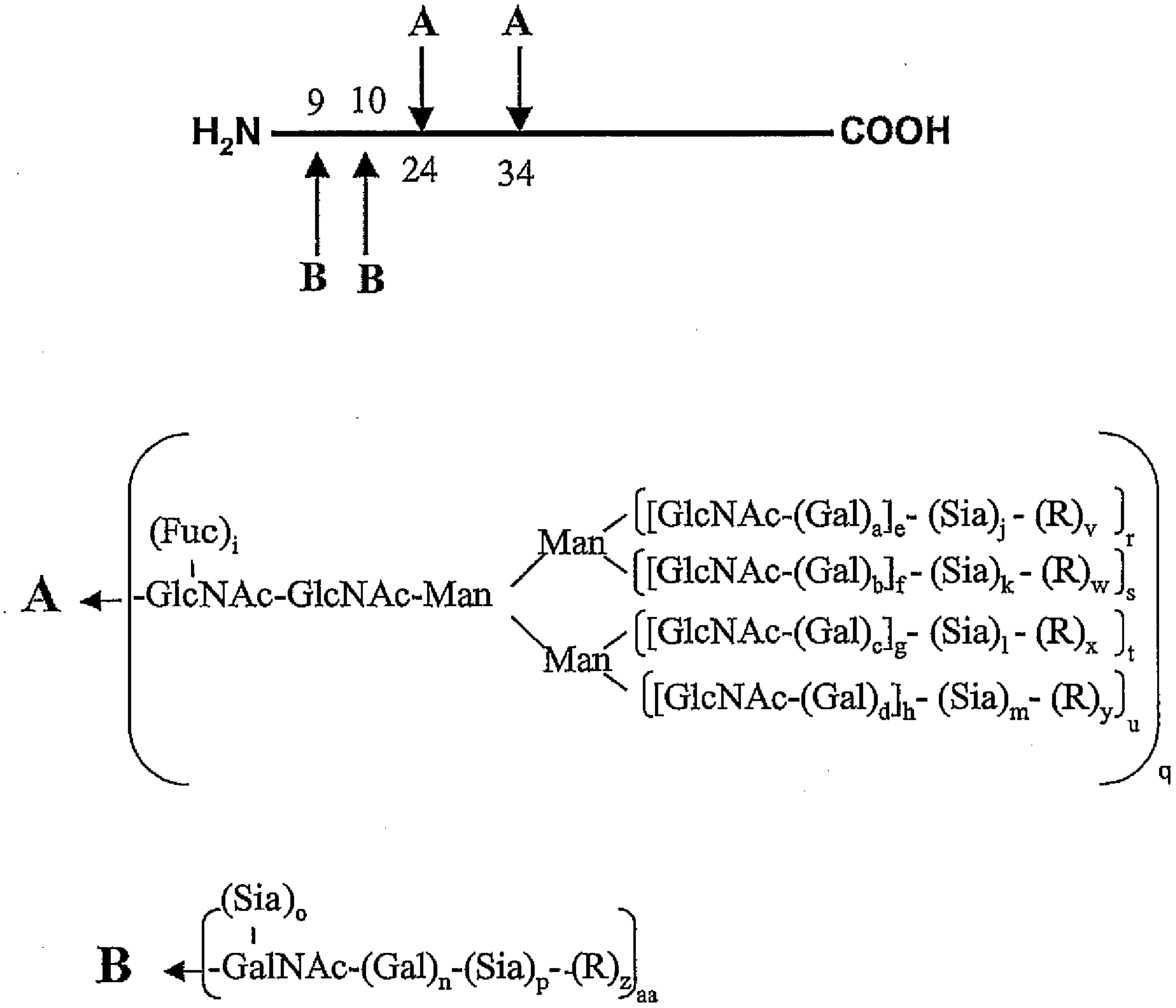
FIG. 33I

CHO, BHK, 293 cells, Vero expressed NESP
a-g, n, q = 1; h = 1 to 3;
j-m, i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 to1; v-z = 0

↓ 1. CMP-SA, poly-α2,8-ST

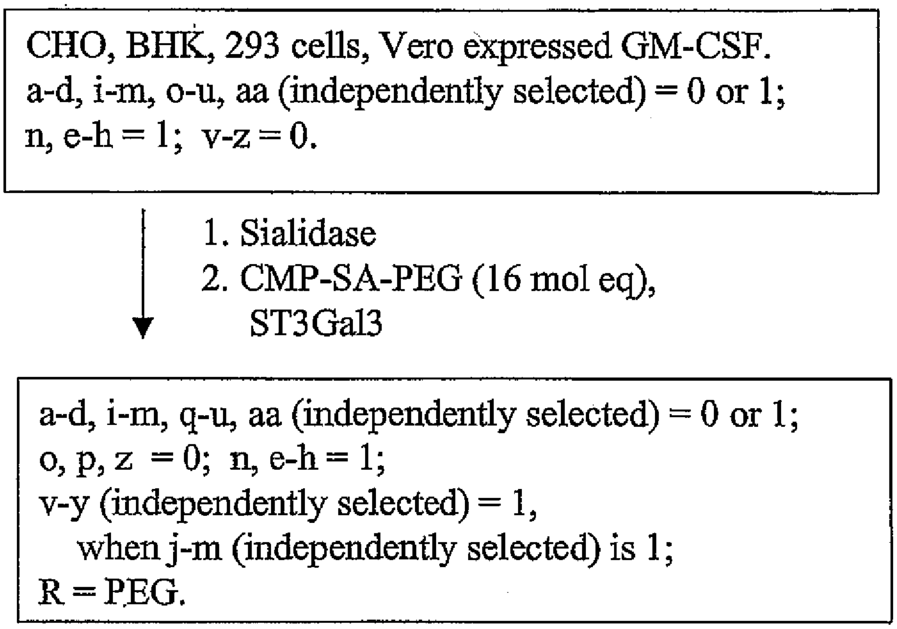
a-g, n, q = 1; h = 1 to 3;
i, j-m, o, p, r-u, (independently selected) = 0 or 1;
v-z (independently selected) = 0-40; R = Sia.

FIG. 33J


A
A
9
10
H_2N
COOH
24
34
B
B
A
$(Fuc)_i$
-GlcNAc-GlcNAc-Man
Man
Man
$[[GlcNAc-(Gal)_a]_e-(Sia)_j-(R)_v]_r$
$[[GlcNAc-(Gal)_b]_f-(Sia)_k-(R)_w]_s$
$[[GlcNAc-(Gal)_c]_g-(Sia)_l-(R)_x]_t$
$[[GlcNAc-(Gal)_d]_h-(Sia)_m-(R)_y]_u$
q
B
$(Sia)_o$
$-GalNAc-(Gal)_n-(Sia)_p-(R)_z$
aa

a-d, i, n-u, aa (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0; R = polymer, glycoconjugate.

FIG. 34A

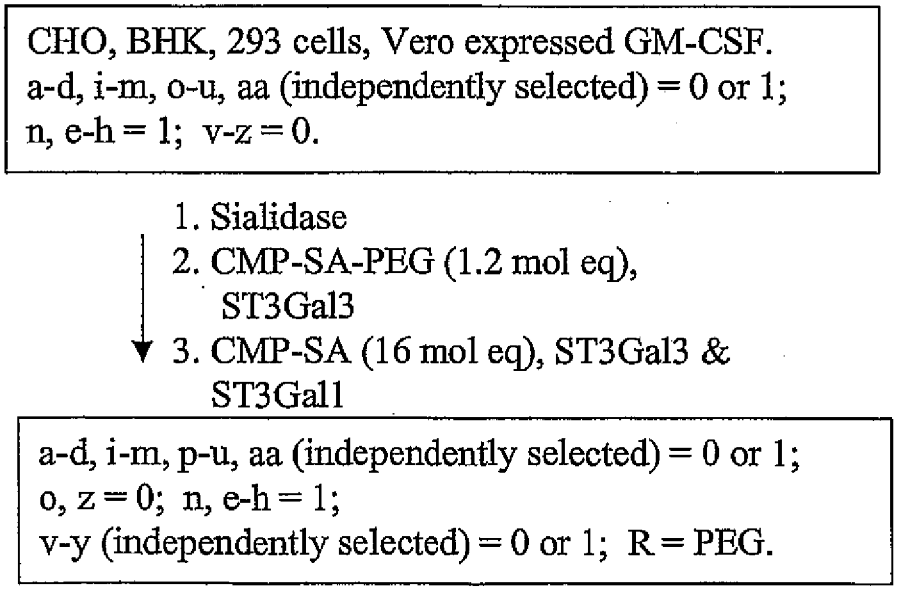


CHO, BHK, 293 cells, Vero expressed GM-CSF.
a-d, i-m, o-u, aa (independently selected) = 0 or 1;
n, e-h = 1; v-z = 0.

1. Sialidase
2. CMP-SA-PEG (16 mol eq), ST3Gal3

a-d, i-m, q-u, aa (independently selected) = 0 or 1;
o, p, z = 0; n, e-h = 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.

FIG. 34B



CHO, BHK, 293 cells, Vero expressed GM-CSF.
a-d, i-m, o-u, aa (independently selected) = 0 or 1;
n, e-h = 1; v-z = 0.

1. Sialidase
2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
3. CMP-SA (16 mol eq), ST3Gal3 & ST3Gal1

a-d, i-m, p-u, aa (independently selected) = 0 or 1;
o, z = 0; n, e-h = 1;
v-y (independently selected) = 0 or 1; R = PEG.

FIG. 34C

NSO expressed GM-CSF.
a-d, i-m, o-u, aa (independently selected) = 0 or 1;
n, e-h = 1; v-z = 0;
Sia (independently selected) = Sia or Gal.

1. Sialidase and α-galactosidase
2. CMP-SA, ST3Gal3
2. CMP-SA-PEG, ST3Gal1

a-d, i-m, p-u, z, aa (independently selected) = 0 or 1;
n, e-h = 1; o, v-y = 0; z = 1, when p = 1; R = PEG.

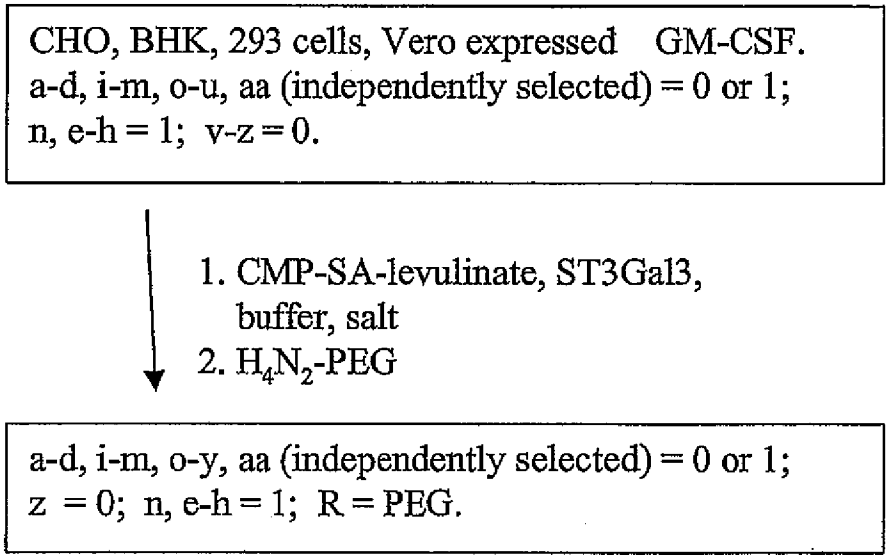
FIG. 34D

CHO, BHK, 293 cells, Vero expressed GM-CSF.
a-d, i-m, o-u, aa (independently selected) = 0 or 1;
n, e-h = 1; v-z = 0.

1. Sialidase
2. CMP-SA-PEG (16 mol eq),
ST3Gal3
3. CMP-SA, ST3Gal3

a-d, i-m, q-y, aa (independently selected) = 0 or 1;
o, p, z = 0; n, e-h = 1; R = PEG.

FIG. 34E

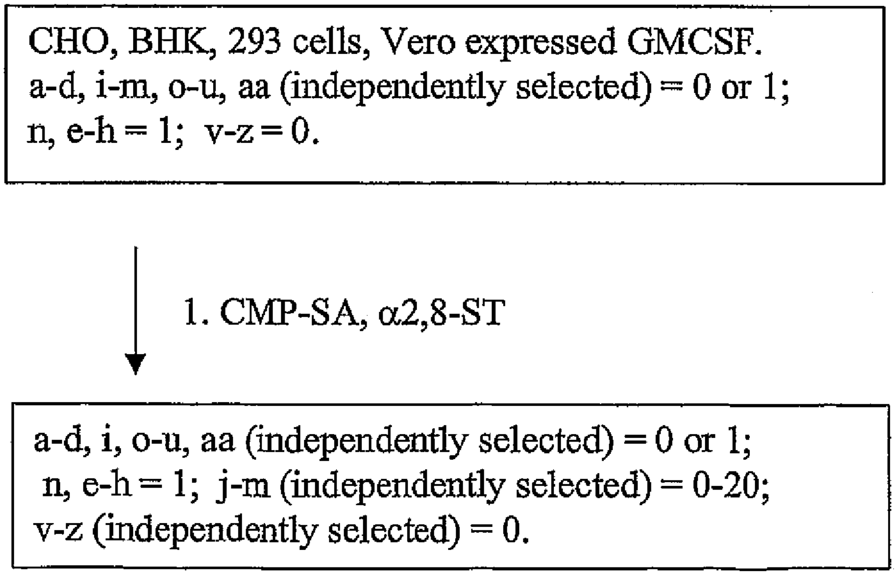


CHO, BHK, 293 cells, Vero expressed GM-CSF.
a-d, i-m, o-u, aa (independently selected) = 0 or 1;
n, e-h = 1; v-z = 0.

1. CMP-SA-levulinate, ST3Gal3, buffer, salt
2. H_4N_2-PEG

a-d, i-m, o-y, aa (independently selected) = 0 or 1;
z = 0; n, e-h = 1; R = PEG.

FIG. 34F

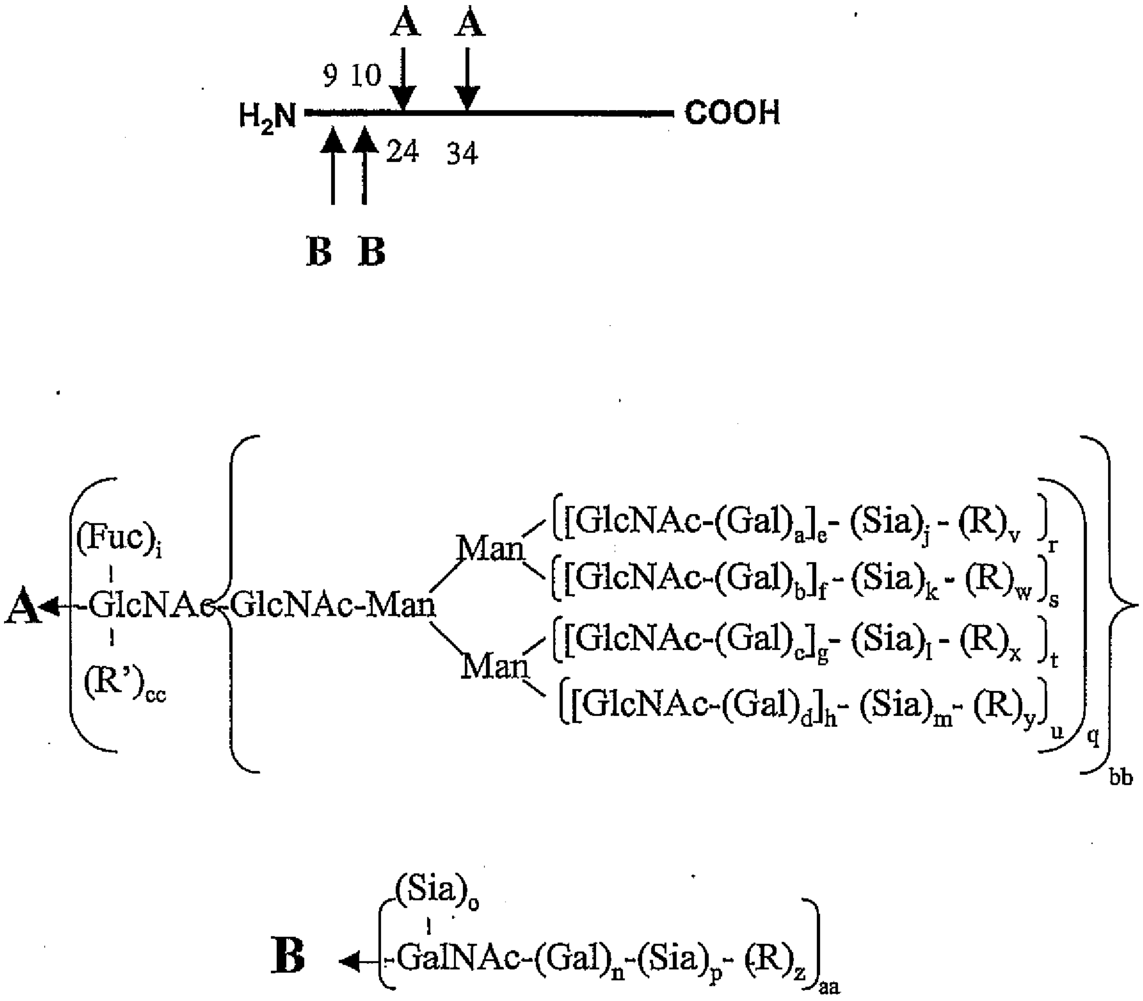


CHO, BHK, 293 cells, Vero expressed GMCSF.
a-d, i-m, o-u, aa (independently selected) = 0 or 1;
n, e-h = 1; v-z = 0.

1. CMP-SA, α2,8-ST

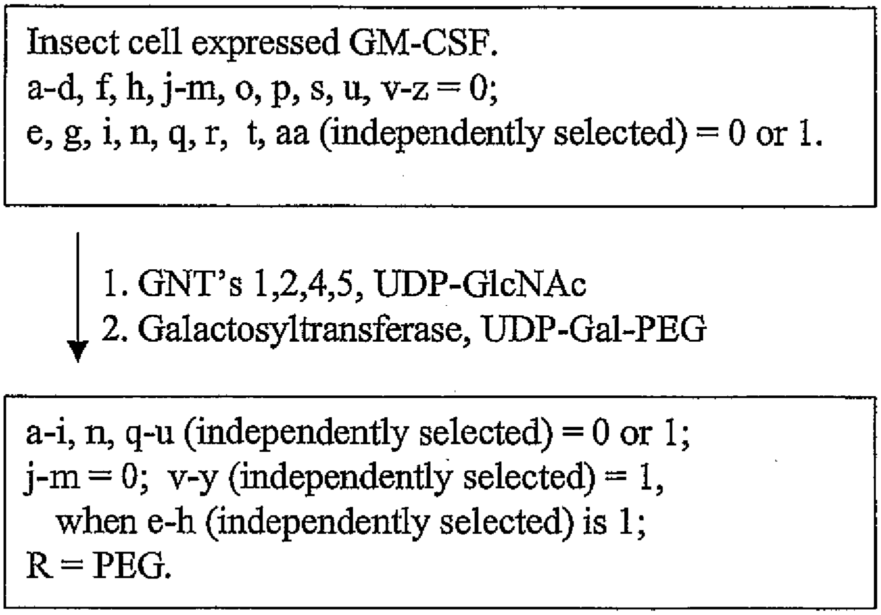
a-d, i, o-u, aa (independently selected) = 0 or 1;
n, e-h = 1; j-m (independently selected) = 0-20;
v-z (independently selected) = 0.

FIG. 34G


A A
9 10
H2N
COOH
24 34
B B
A
(Fuc)i
-GlcNAc-GlcNAc-Man
(R')cc
Man
[GlcNAc-(Gal)a]e- (Sia)j - (R)v r
[GlcNAc-(Gal)b]f - (Sia)k - (R)w s
Man
[GlcNAc-(Gal)c]g- (Sia)l - (R)x t
[GlcNAc-(Gal)d]h- (Sia)m- (R)y u
q
bb
B
(Sia)o
-GalNAc-(Gal)n-(Sia)p- (R)z
aa

a-d, i, n-u, aa, bb, cc (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0; R = modifying group, mannose, oligo-mannose.
R'= H, glycosyl residue, modifying group. glycoconjugate.

FIG. 34H

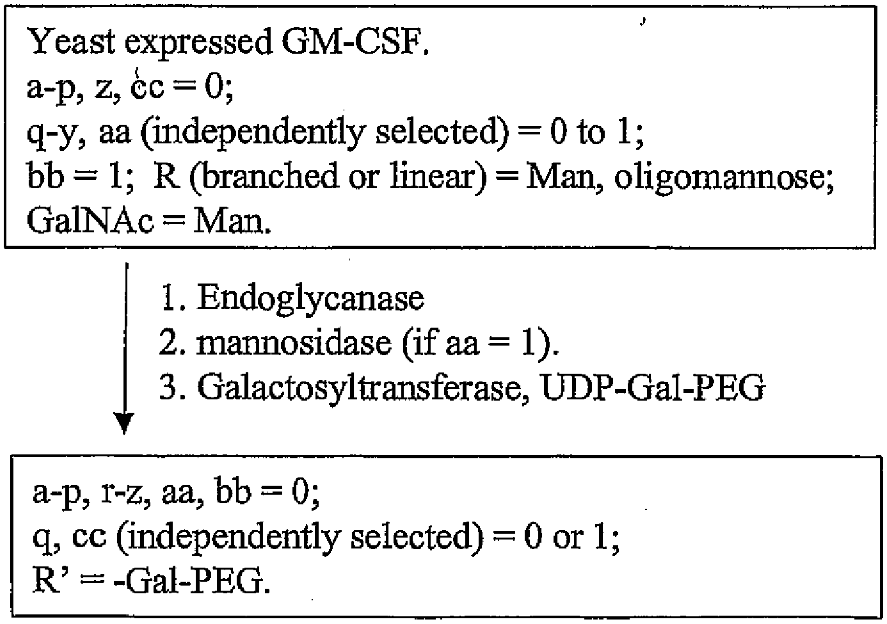


Insect cell expressed GM-CSF.
a-d, f, h, j-m, o, p, s, u, v-z = 0;
e, g, i, n, q, r, t, aa (independently selected) = 0 or 1.

1. GNT's 1,2,4,5, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal-PEG

a-i, n, q-u (independently selected) = 0 or 1;
j-m = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.

FIG. 34I



Yeast expressed GM-CSF.
a-p, z, cc = 0;
q-y, aa (independently selected) = 0 to 1;
bb = 1; R (branched or linear) = Man, oligomannose;
GalNAc = Man.

1. Endoglycanase
2. mannosidase (if aa = 1).
3. Galactosyltransferase, UDP-Gal-PEG

a-p, r-z, aa, bb = 0;
q, cc (independently selected) = 0 or 1;
R' = -Gal-PEG.

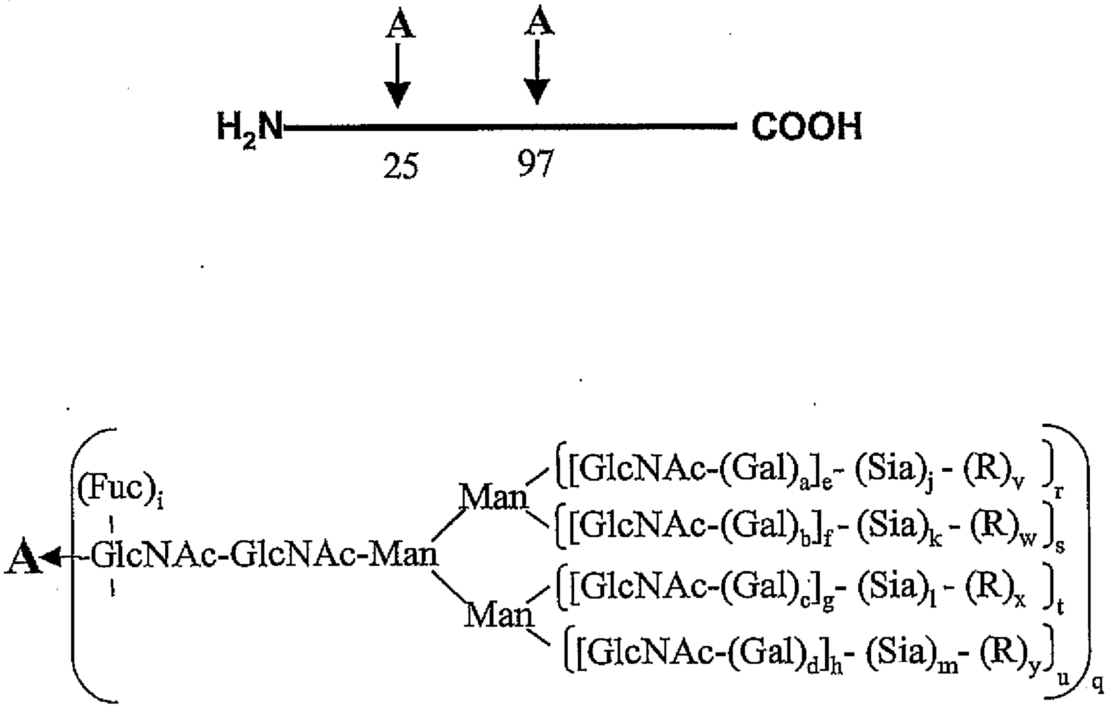
FIG. 34J

CHO, BHK, 293 cells, Vero expressed GM-CSF.
a--m, o-u, aa, bb (independently selected) = 0 or 1;
n, v-z, cc = 0.

1. sialidase
2. CMP-SA, ST3Gal3
2. CMP-SA-linker-SA-CMP, ST3Gal1
3. ST3Gal3, transferrin

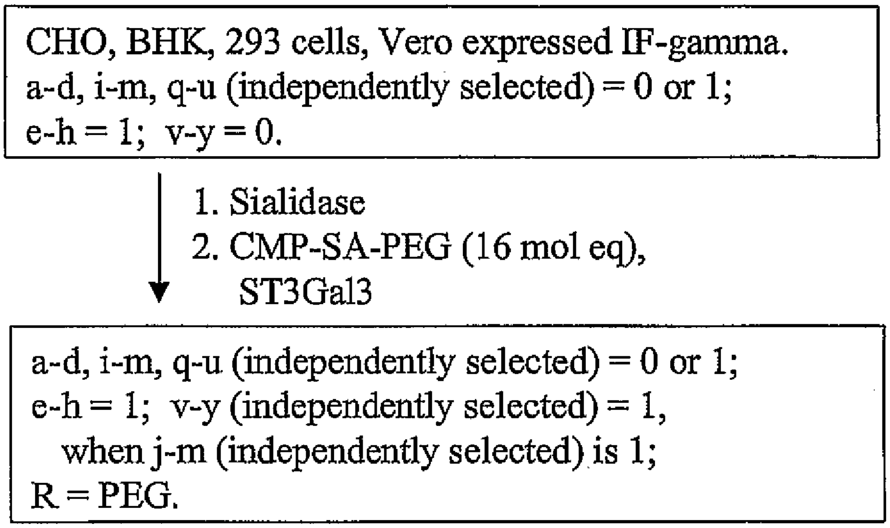
a--m, p-u, z, aa (independently selected) = 0 or 1;
o, v-y, cc = 0; bb, n = 1; R = transferrin.

FIG. 34K


A
A
H2N
COOH
25
97
(Fuc)i
A
GlcNAc-GlcNAc-Man
Man
Man
[[GlcNAc-(Gal)a]e- (Sia)j - (R)v]r
[[GlcNAc-(Gal)b]f - (Sia)k - (R)w]s
[[GlcNAc-(Gal)c]g- (Sia)l - (R)x]t
[[GlcNAc-(Gal)d]h- (Sia)m- (R)y]u
q

a-d, i, q-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0; R = polymer.

FIG. 35A

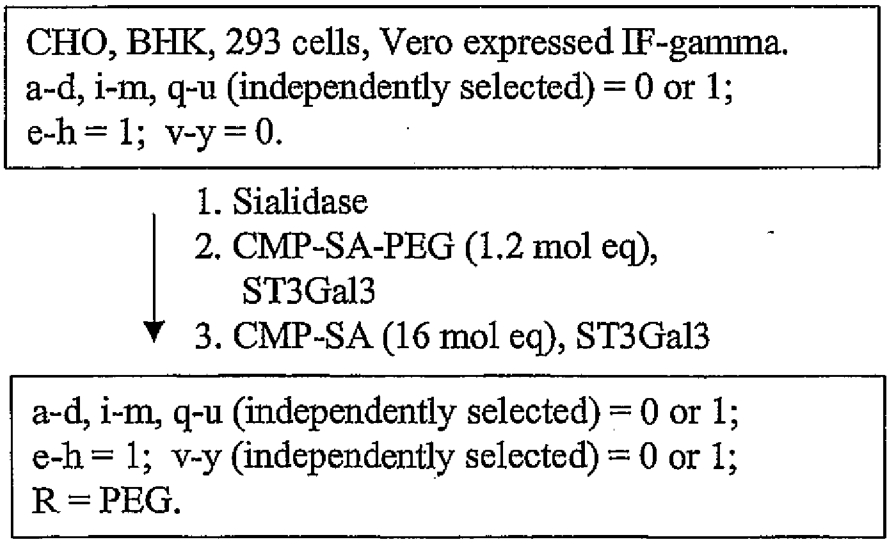


CHO, BHK, 293 cells, Vero expressed IF-gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. Sialidase
2. CMP-SA-PEG (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.

FIG. 35B

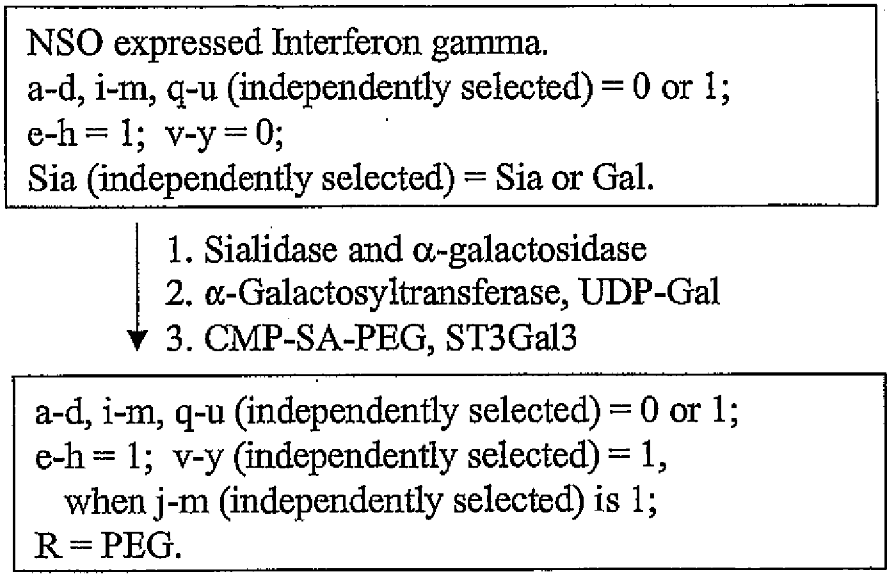


CHO, BHK, 293 cells, Vero expressed IF-gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. Sialidase
2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
3. CMP-SA (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 35C

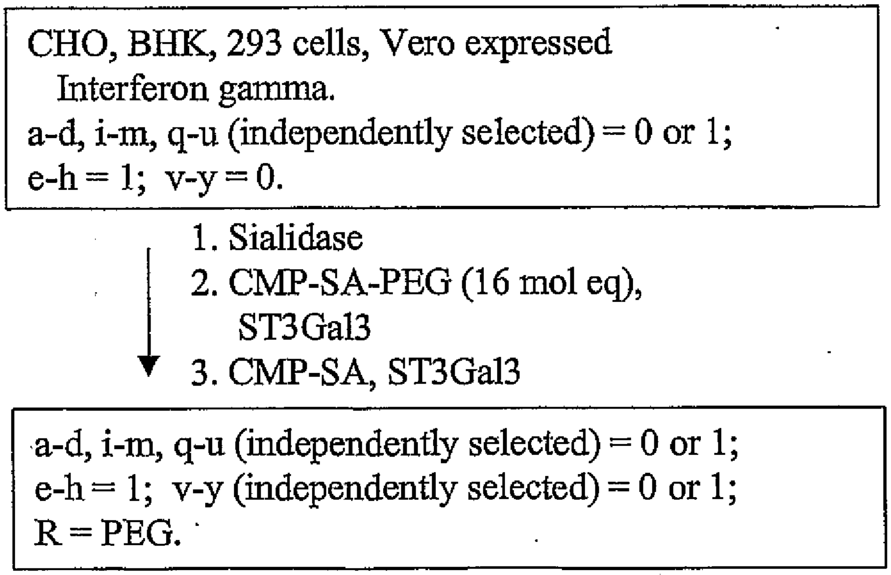


NSO expressed Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0;
Sia (independently selected) = Sia or Gal.

1. Sialidase and α-galactosidase
2. α-Galactosyltransferase, UDP-Gal
3. CMP-SA-PEG, ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.

FIG. 35D

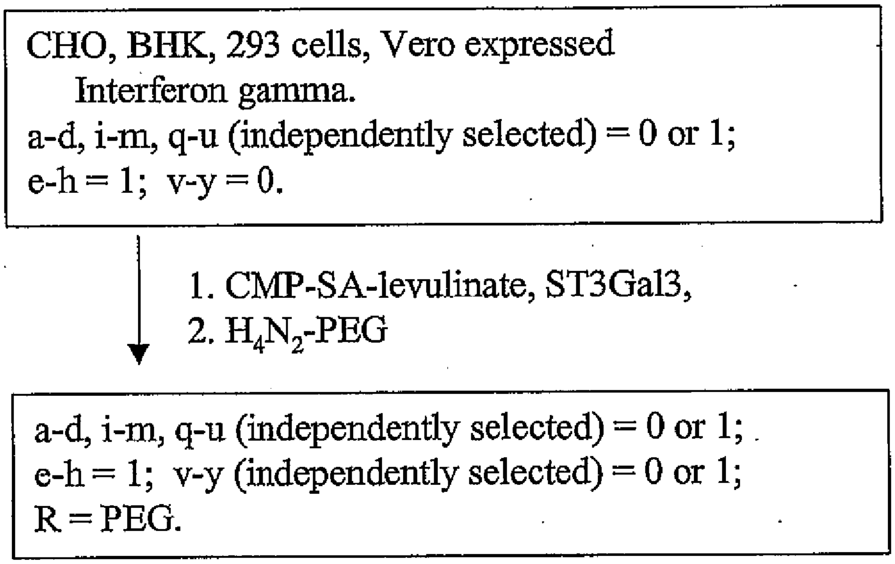


CHO, BHK, 293 cells, Vero expressed
Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. Sialidase
2. CMP-SA-PEG (16 mol eq),
ST3Gal3
3. CMP-SA, ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 35E

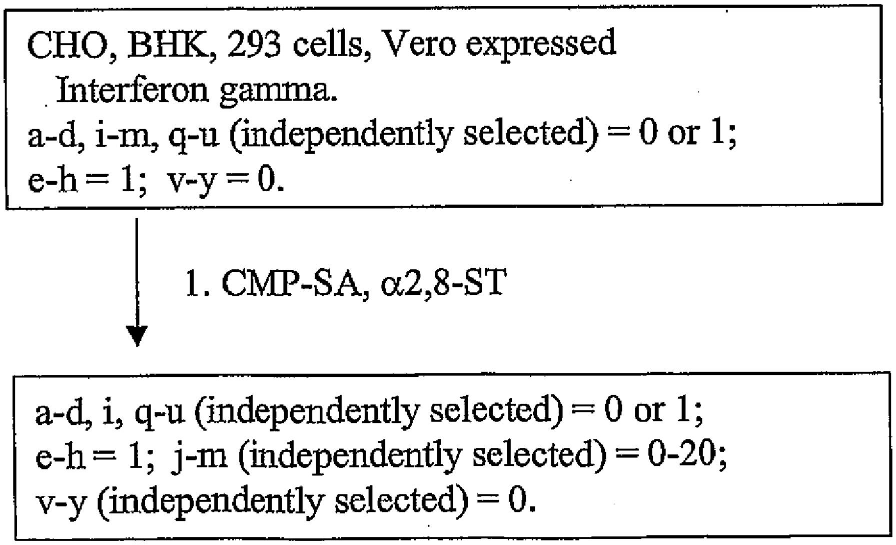


CHO, BHK, 293 cells, Vero expressed Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. CMP-SA-levulinate, ST3Gal3,
2. H_4N_2-PEG

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 35F

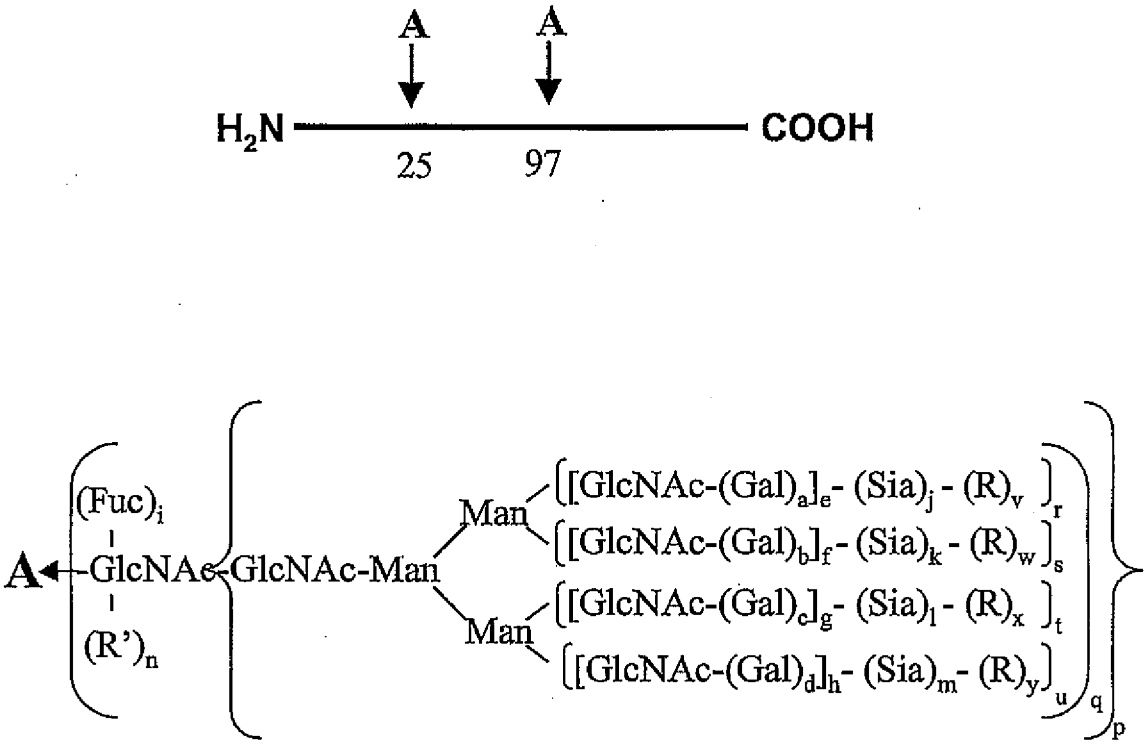


CHO, BHK, 293 cells, Vero expressed Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. CMP-SA, α2,8-ST

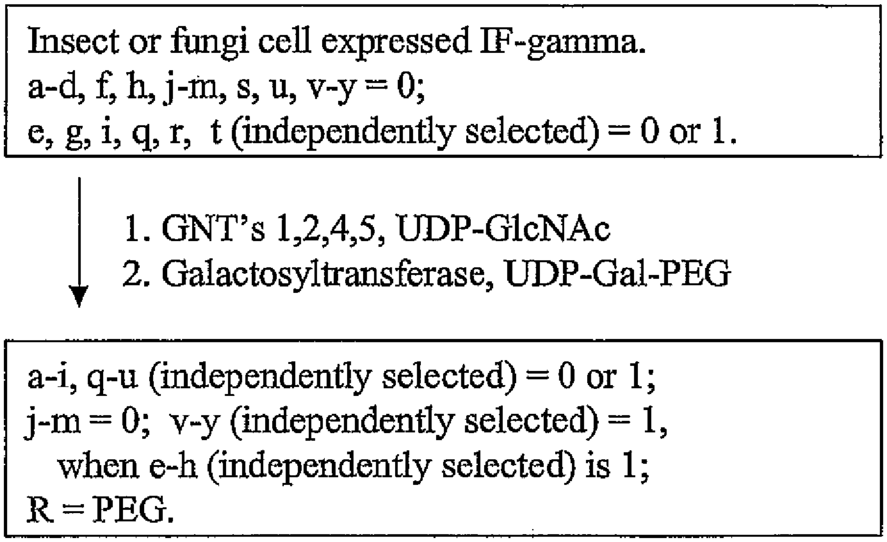
a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1; j-m (independently selected) = 0-20;
v-y (independently selected) = 0.

FIG. 35G


A
A
H2N
COOH
25
97
A
(Fuc)i
GlcNAc
(R')n
GlcNAc-Man
Man
[[GlcNAc-(Gal)a]e- (Sia)j - (R)v]r
[[GlcNAc-(Gal)b]f- (Sia)k - (R)w]s
Man
[[GlcNAc-(Gal)c]g- (Sia)l - (R)x]t
[[GlcNAc-(Gal)d]h- (Sia)m- (R)y]u
q
p

a-d, i, n, p-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0;
R = modifying group, mannose, oligo-mannose;
R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 35H

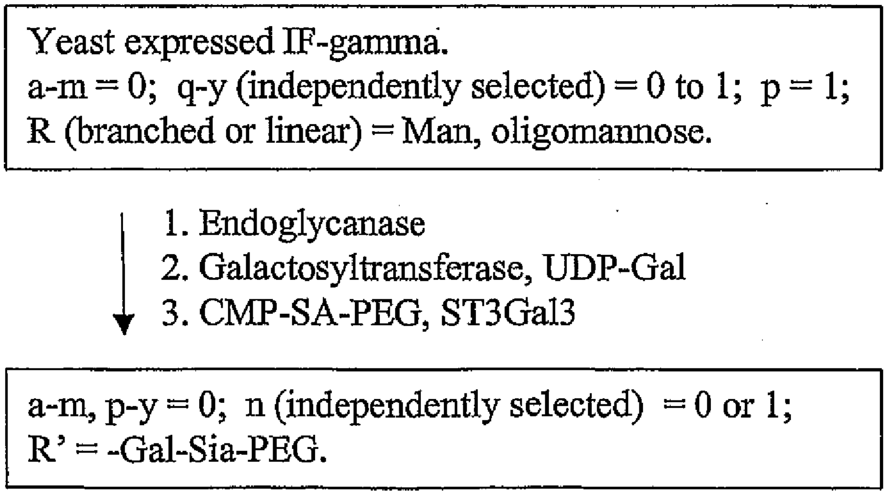


Insect or fungi cell expressed IF-gamma.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.

1. GNT's 1,2,4,5, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal-PEG

a-i, q-u (independently selected) = 0 or 1;
j-m = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.

FIG. 35I

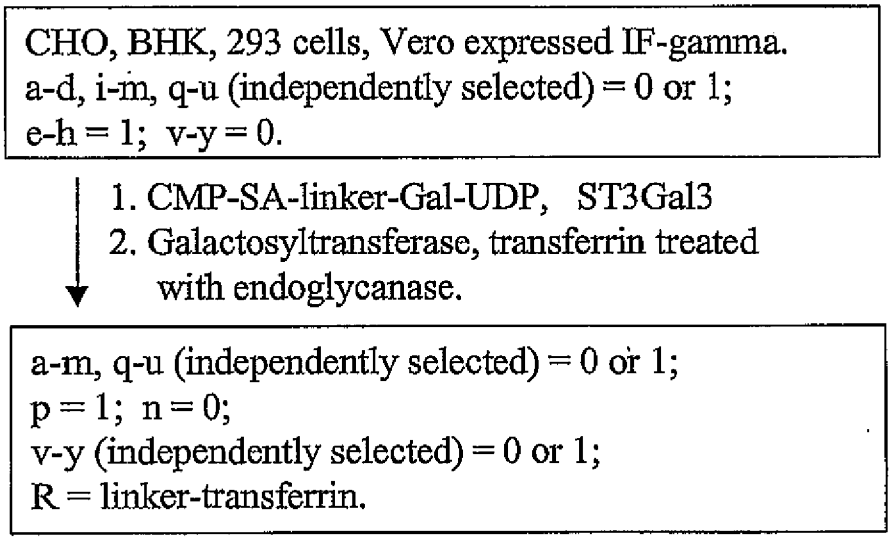


Yeast expressed IF-gamma.
a-m = 0; q-y (independently selected) = 0 to 1; p = 1;
R (branched or linear) = Man, oligomannose.

1. Endoglycanase
2. Galactosyltransferase, UDP-Gal
3. CMP-SA-PEG, ST3Gal3

a-m, p-y = 0; n (independently selected) = 0 or 1;
R' = -Gal-Sia-PEG.

FIG. 35J

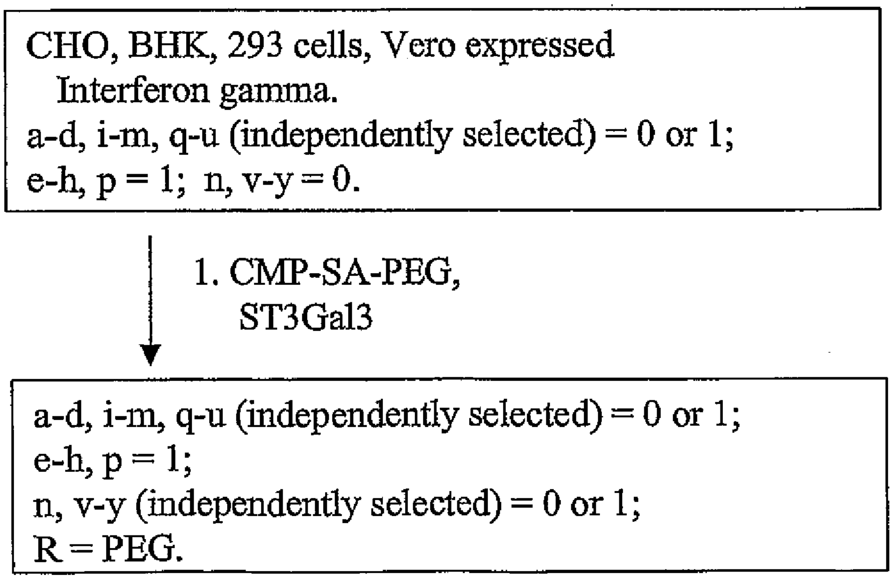


CHO, BHK, 293 cells, Vero expressed IF-gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. CMP-SA-linker-Gal-UDP, ST3Gal3
2. Galactosyltransferase, transferrin treated with endoglycanase.

a-m, q-u (independently selected) = 0 or 1;
p = 1; n = 0;
v-y (independently selected) = 0 or 1;
R = linker-transferrin.

FIG. 35K

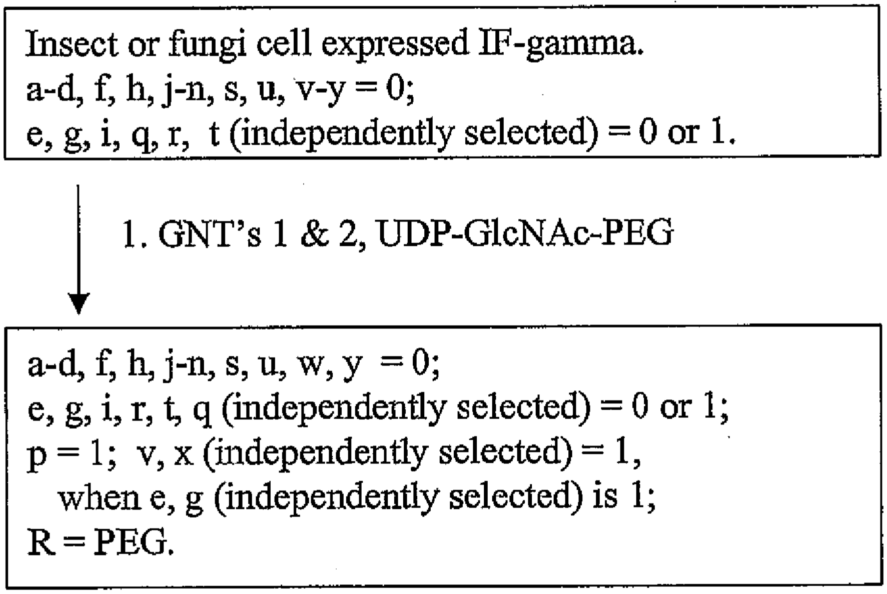


CHO, BHK, 293 cells, Vero expressed Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h, p = 1; n, v-y = 0.

1. CMP-SA-PEG, ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h, p = 1;
n, v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 35L

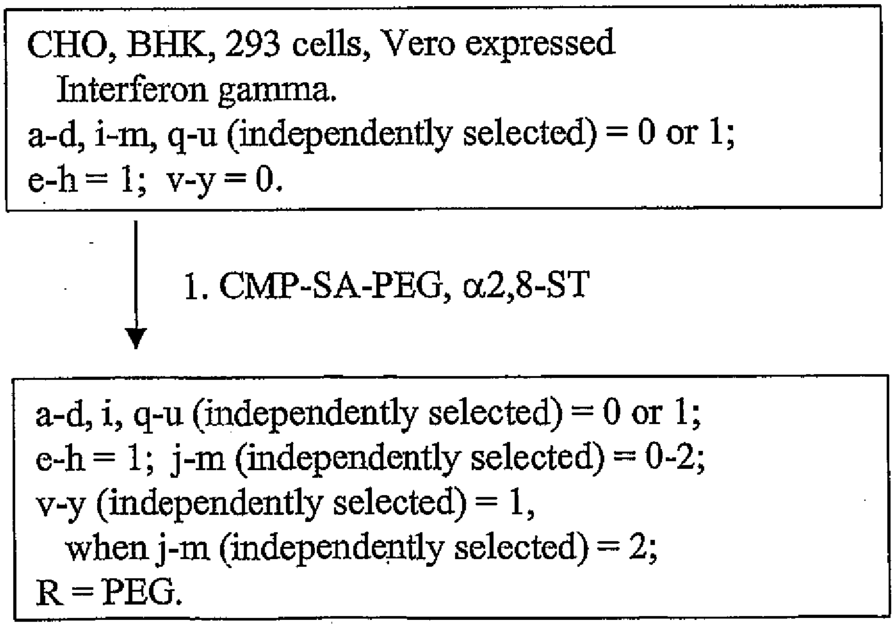


Insect or fungi cell expressed IF-gamma.
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.

1. GNT's 1 & 2, UDP-GlcNAc-PEG

a-d, f, h, j-n, s, u, w, y = 0;
e, g, i, r, t, q (independently selected) = 0 or 1;
p = 1; v, x (independently selected) = 1,
when e, g (independently selected) is 1;
R = PEG.

FIG. 35M

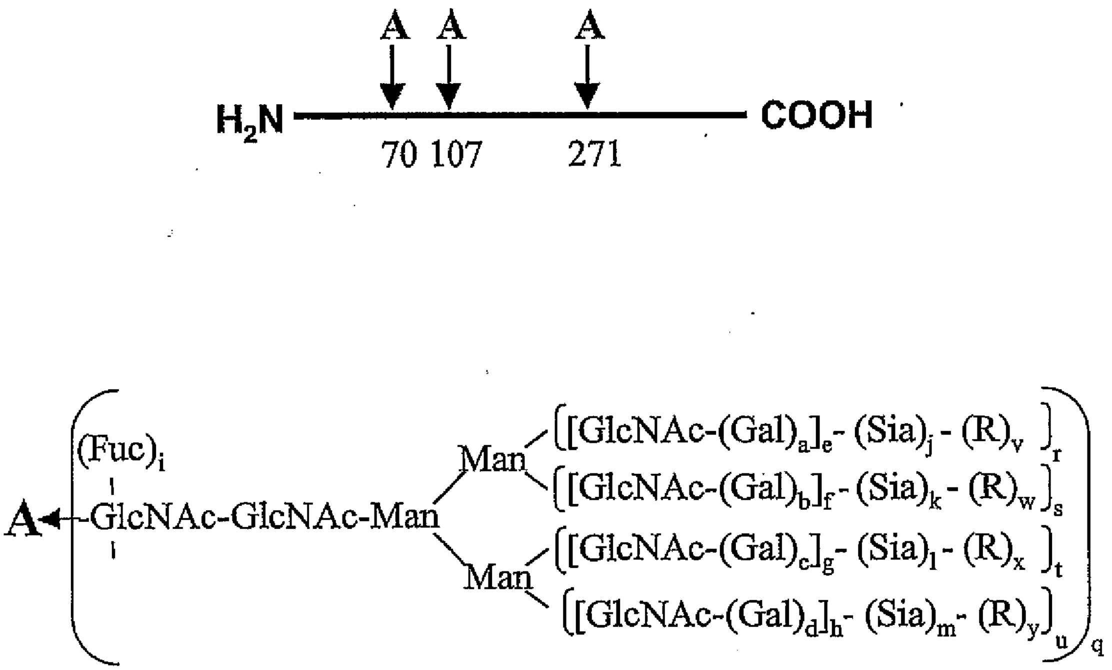


CHO, BHK, 293 cells, Vero expressed
Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. CMP-SA-PEG, α2,8-ST

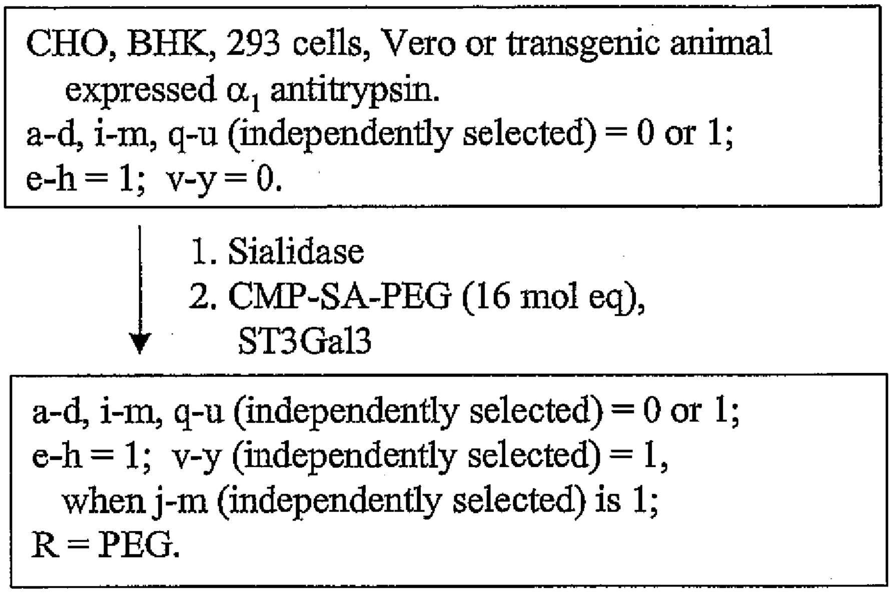
a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1; j-m (independently selected) = 0-2;
v-y (independently selected) = 1,
when j-m (independently selected) = 2;
R = PEG.

FIG. 35N


A
A
A
H2N
COOH
70
107
271
A
(Fuc)i
GlcNAc-GlcNAc-Man
Man
Man
[[GlcNAc-(Gal)a]e- (Sia)j - (R)v]r
[[GlcNAc-(Gal)b]f - (Sia)k - (R)w]s
[[GlcNAc-(Gal)c]g- (Sia)l - (R)x]t
[[GlcNAc-(Gal)d]h- (Sia)m- (R)y]u
q

a-d, i, q-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0; R = polymer.

FIG. 36A

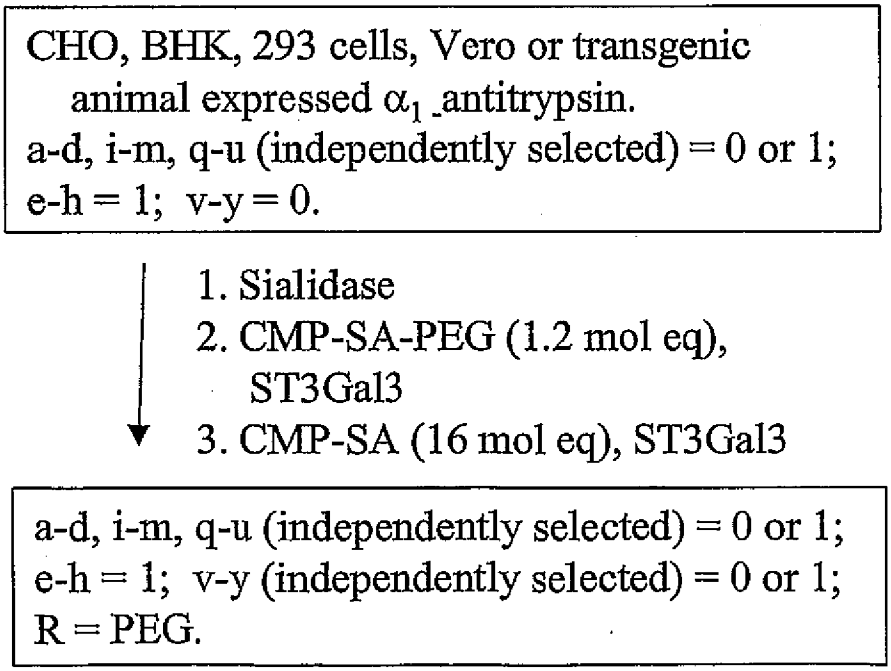


CHO, BHK, 293 cells, Vero or transgenic animal expressed α_1 antitrypsin.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. Sialidase
2. CMP-SA-PEG (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1, when j-m (independently selected) is 1;
R = PEG.

FIG. 36B

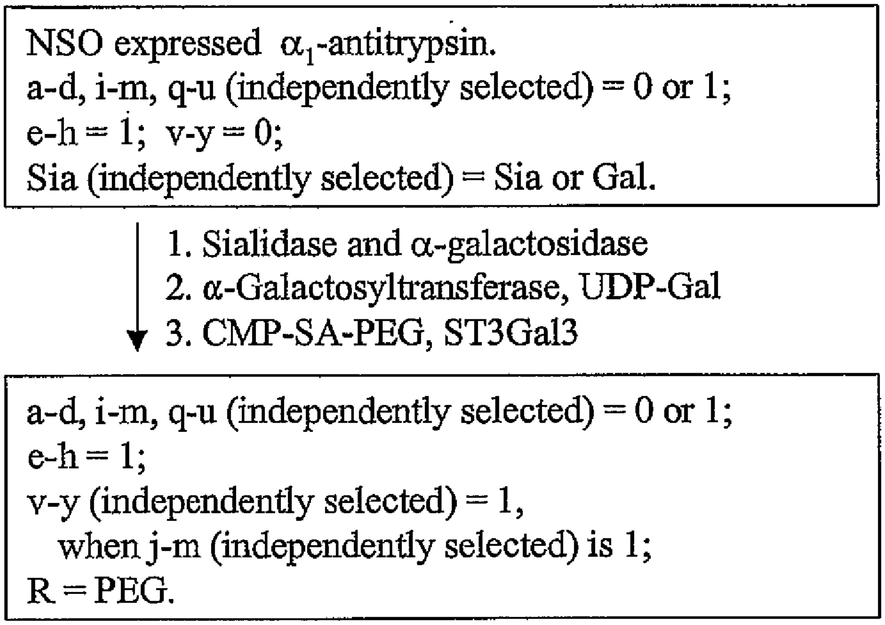


CHO, BHK, 293 cells, Vero or transgenic animal expressed α_1 antitrypsin.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. Sialidase
2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
3. CMP-SA (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 36C

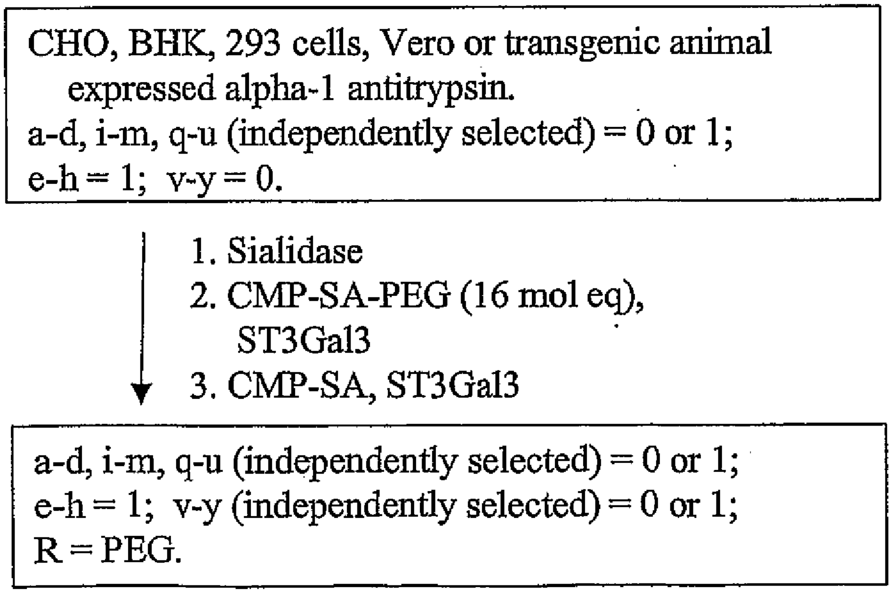


NSO expressed α_1-antitrypsin.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0;
Sia (independently selected) = Sia or Gal.

1. Sialidase and α-galactosidase
2. α-Galactosyltransferase, UDP-Gal
3. CMP-SA-PEG, ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.

FIG. 36D

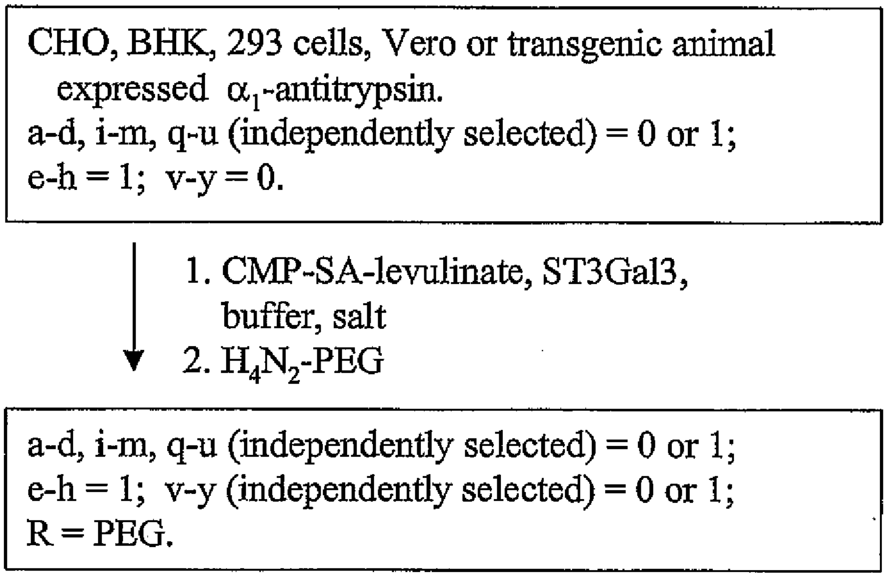


CHO, BHK, 293 cells, Vero or transgenic animal expressed alpha-1 antitrypsin.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. Sialidase
2. CMP-SA-PEG (16 mol eq), ST3Gal3
3. CMP-SA, ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 36E

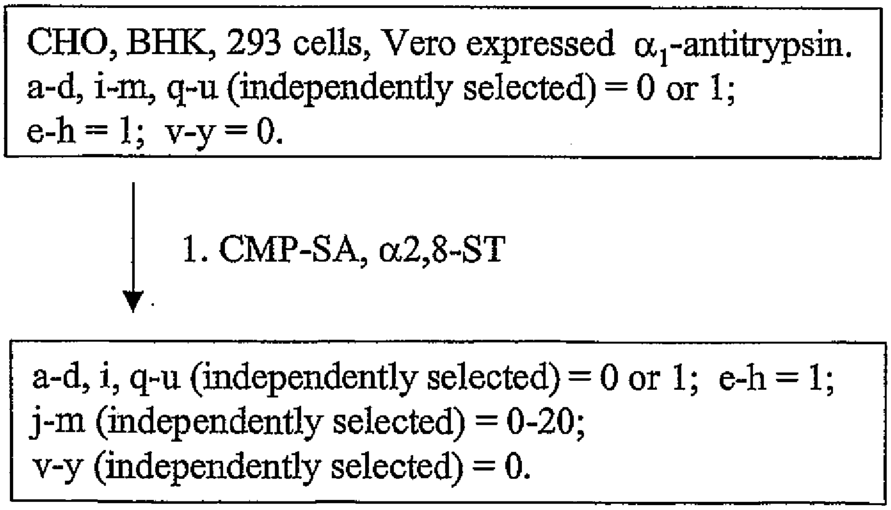


CHO, BHK, 293 cells, Vero or transgenic animal expressed α_1-antitrypsin.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. CMP-SA-levulinate, ST3Gal3, buffer, salt
2. H_4N_2-PEG

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 36F

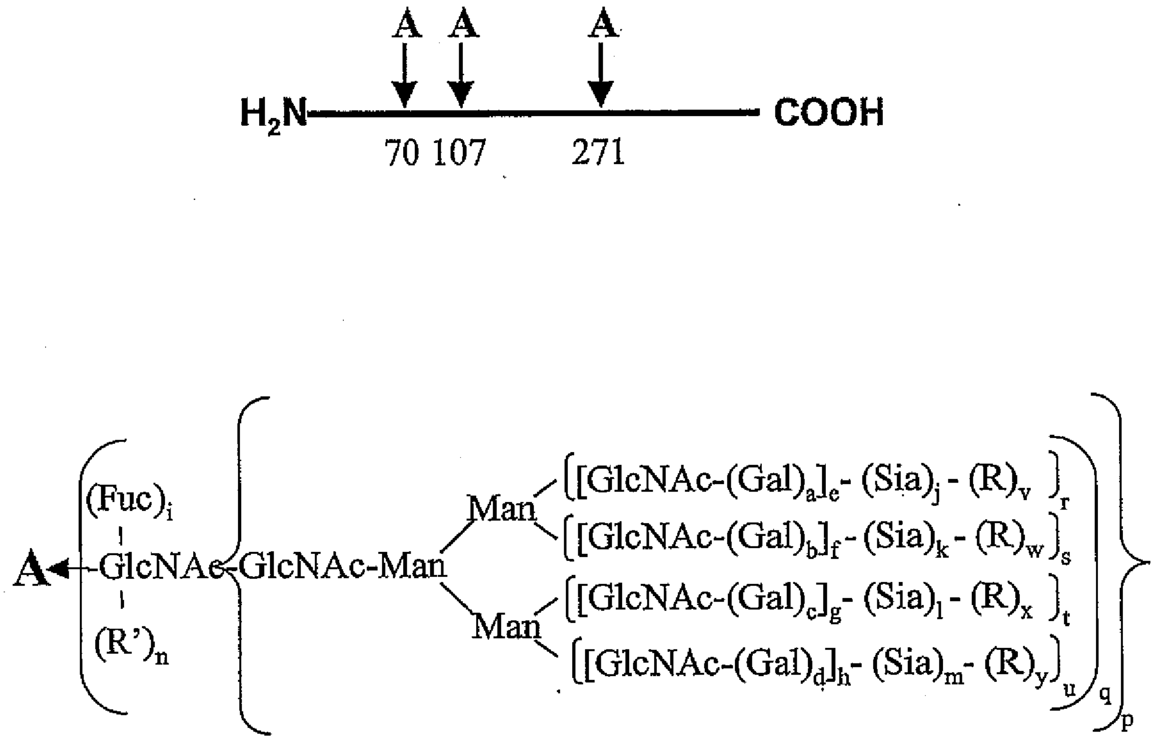


CHO, BHK, 293 cells, Vero expressed α_1-antitrypsin.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. CMP-SA, α2,8-ST

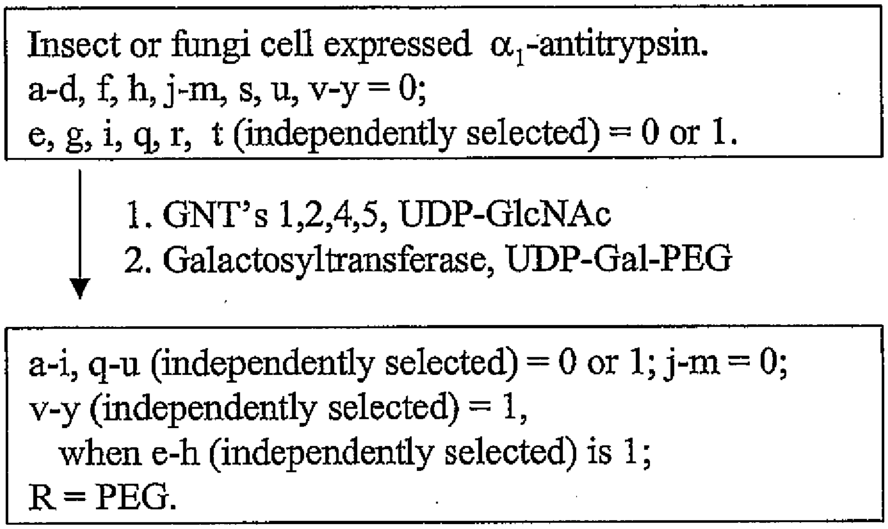
a-d, i, q-u (independently selected) = 0 or 1; e-h = 1;
j-m (independently selected) = 0-20;
v-y (independently selected) = 0.

FIG. 36G


A
A
A
H2N
COOH
70
107
271
A
(Fuc)i
GlcNAc
(R')n
GlcNAc-Man
Man
Man
[[GlcNAc-(Gal)a]e- (Sia)j - (R)v]r
[[GlcNAc-(Gal)b]f - (Sia)k - (R)w]s
[[GlcNAc-(Gal)c]g- (Sia)l - (R)x]t
[[GlcNAc-(Gal)d]h- (Sia)m- (R)y]u
q
p

a-d, i, n, p-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0;
R = modifying group, mannose, oligo-mannose;
R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 36H

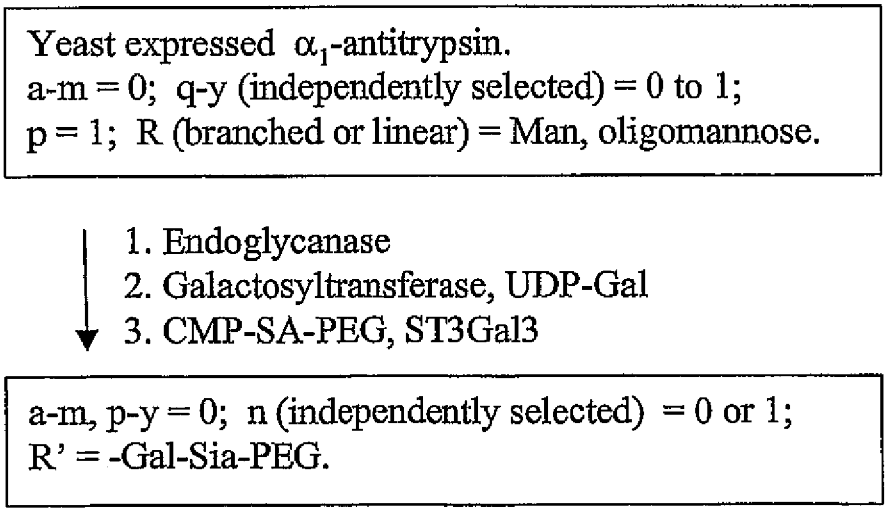


Insect or fungi cell expressed α_1-antitrypsin.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.

1. GNT's 1,2,4,5, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal-PEG

a-i, q-u (independently selected) = 0 or 1; j-m = 0;
v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.

FIG. 36I



Yeast expressed α_1-antitrypsin.
a-m = 0; q-y (independently selected) = 0 to 1;
p = 1; R (branched or linear) = Man, oligomannose.

1. Endoglycanase
2. Galactosyltransferase, UDP-Gal
3. CMP-SA-PEG, ST3Gal3

a-m, p-y = 0; n (independently selected) = 0 or 1;
R' = -Gal-Sia-PEG.

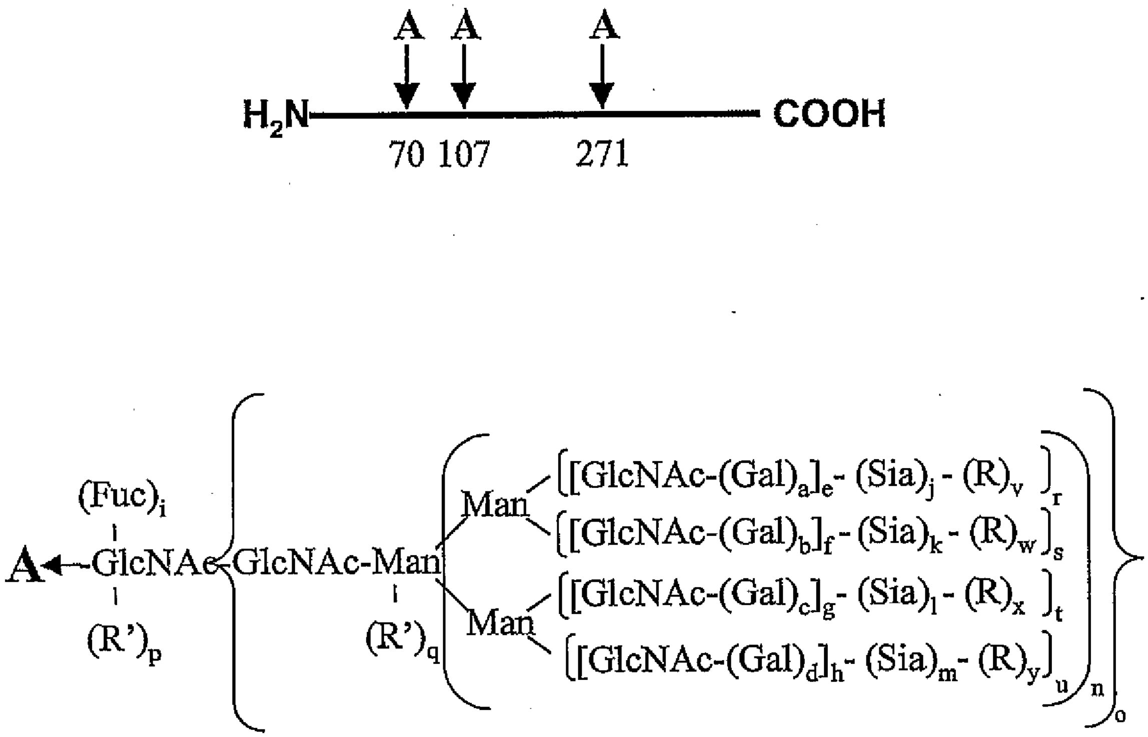
FIG. 36J

CHO, BHK, 293 cells, Vero expressed α_1-antitrypsin.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. CMP-SA-linker-Gal-UDP, ST3Gal3
2. Galactosyltransferase, transferrin treated with endoglycanase

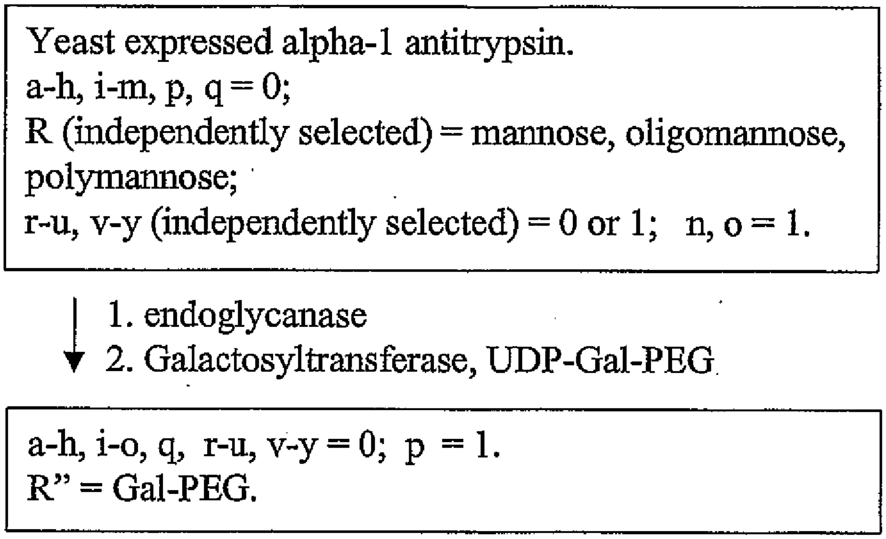
a-m, q-u (independently selected) = 0 or 1;
p = 1; n = 0;
v-y (independently selected) = 0 or 1;
R = linker-transferrin.

FIG. 36K


A
A
A
H2N
COOH
70
107
271
(Fuc)i
A
GlcNAc
(R')p
GlcNAc-Man
(R')q
Man
Man
[[GlcNAc-(Gal)a]e- (Sia)j - (R)v]r
[[GlcNAc-(Gal)b]f - (Sia)k - (R)w]s
[[GlcNAc-(Gal)c]g- (Sia)l - (R)x]t
[[GlcNAc-(Gal)d]h- (Sia)m- (R)y]u
n
o

a-d, i, n-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
j-m (independently selected) = 0 to 20.
R = polymer;
R', R" (independently selected) = sugar, glycoconjugate.

FIG. 36L

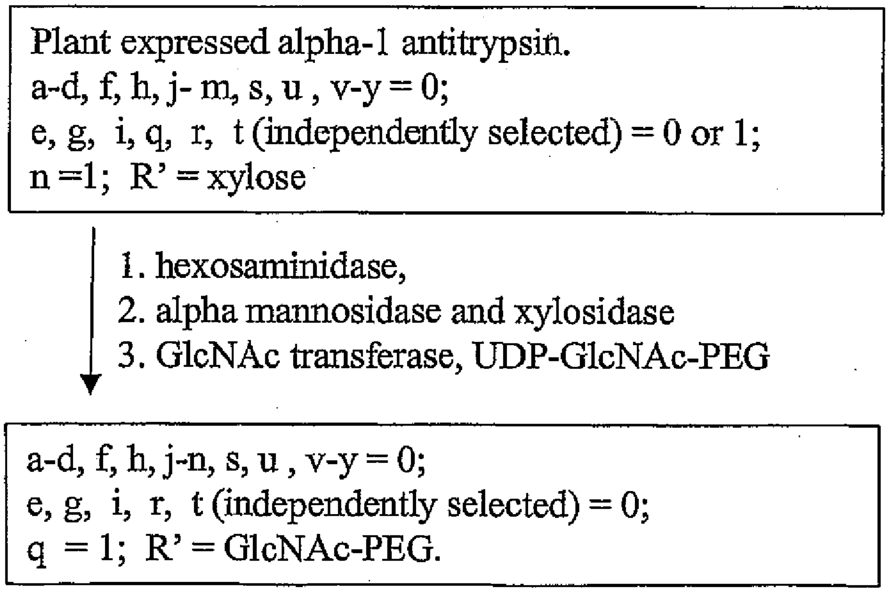


Yeast expressed alpha-1 antitrypsin.
a-h, i-m, p, q = 0;
R (independently selected) = mannose, oligomannose, polymannose;
r-u, v-y (independently selected) = 0 or 1; n, o = 1.

1. endoglycanase
2. Galactosyltransferase, UDP-Gal-PEG

a-h, i-o, q, r-u, v-y = 0; p = 1.
R" = Gal-PEG.

FIG. 36M

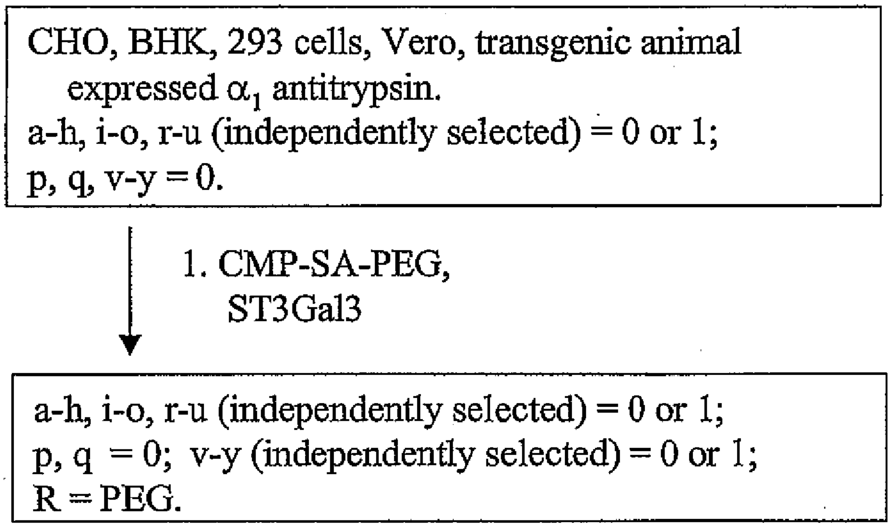


Plant expressed alpha-1 antitrypsin.
a-d, f, h, j- m, s, u , v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1;
n =1; R' = xylose

1. hexosaminidase,
2. alpha mannosidase and xylosidase
3. GlcNAc transferase, UDP-GlcNAc-PEG

a-d, f, h, j-n, s, u , v-y = 0;
e, g, i, r, t (independently selected) = 0;
q = 1; R' = GlcNAc-PEG.

FIG. 36N

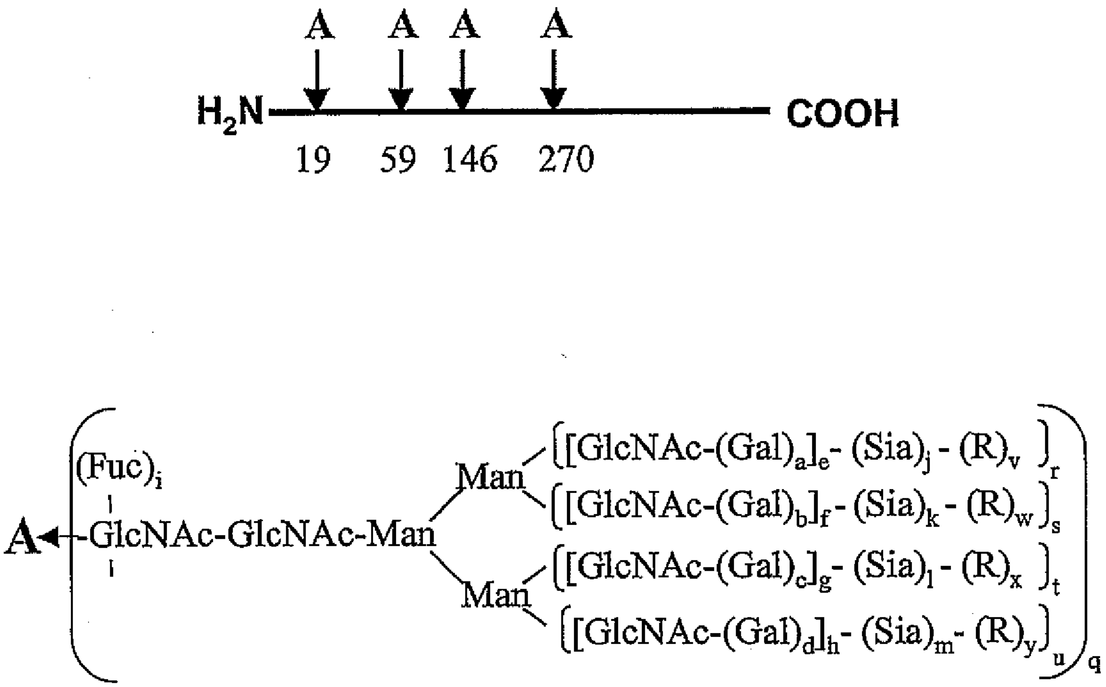


CHO, BHK, 293 cells, Vero, transgenic animal expressed α_1 antitrypsin.
a-h, i-o, r-u (independently selected) = 0 or 1;
p, q, v-y = 0.

1. CMP-SA-PEG, ST3Gal3

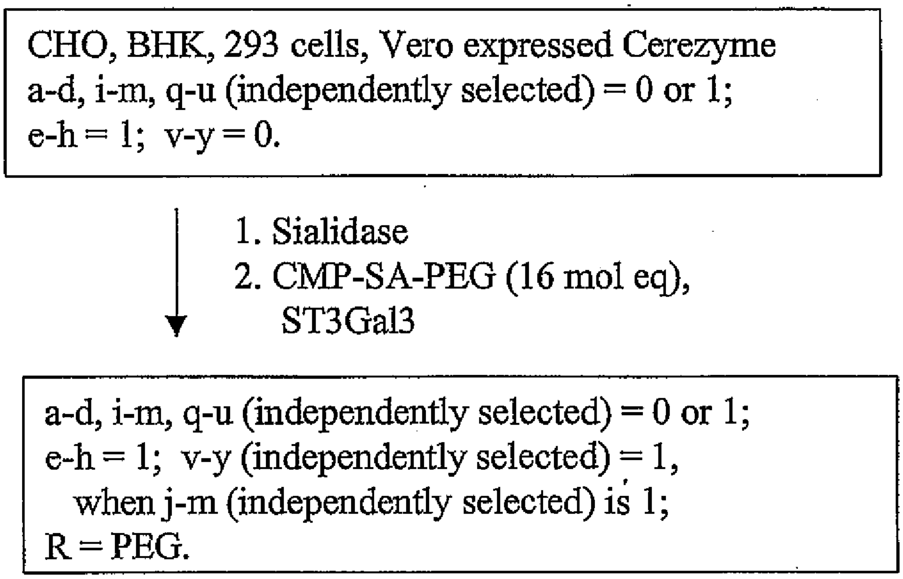
a-h, i-o, r-u (independently selected) = 0 or 1;
p, q = 0; v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 36O


A
A
A
A
H2N
COOH
19
59
146
270
A
(Fuc)i
GlcNAc-GlcNAc-Man
Man
Man
[[GlcNAc-(Gal)a]e- (Sia)j - (R)v]r
[[GlcNAc-(Gal)b]f - (Sia)k - (R)w]s
[[GlcNAc-(Gal)c]g- (Sia)l - (R)x]t
[[GlcNAc-(Gal)d]h- (Sia)m- (R)y]u
q

a-d, i, q-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0; R = polymer.

FIG. 37A

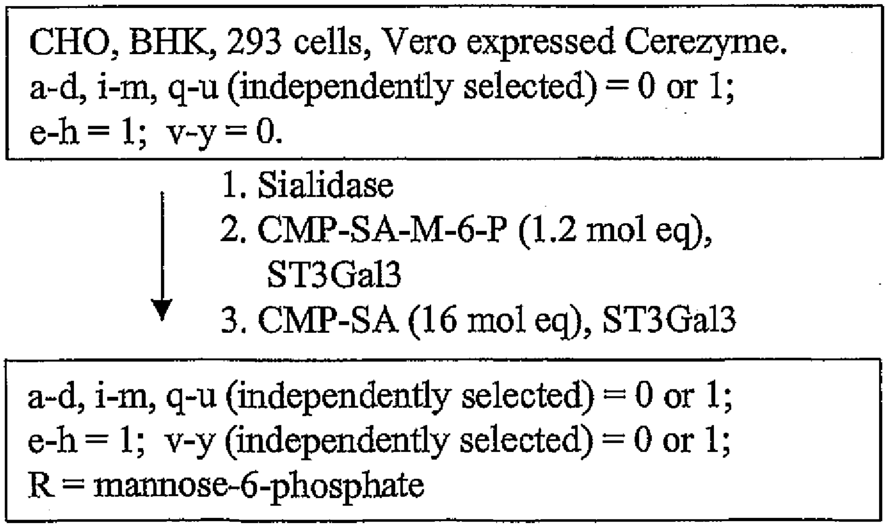


CHO, BHK, 293 cells, Vero expressed Cerezyme
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. Sialidase
2. CMP-SA-PEG (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.

FIG. 37B

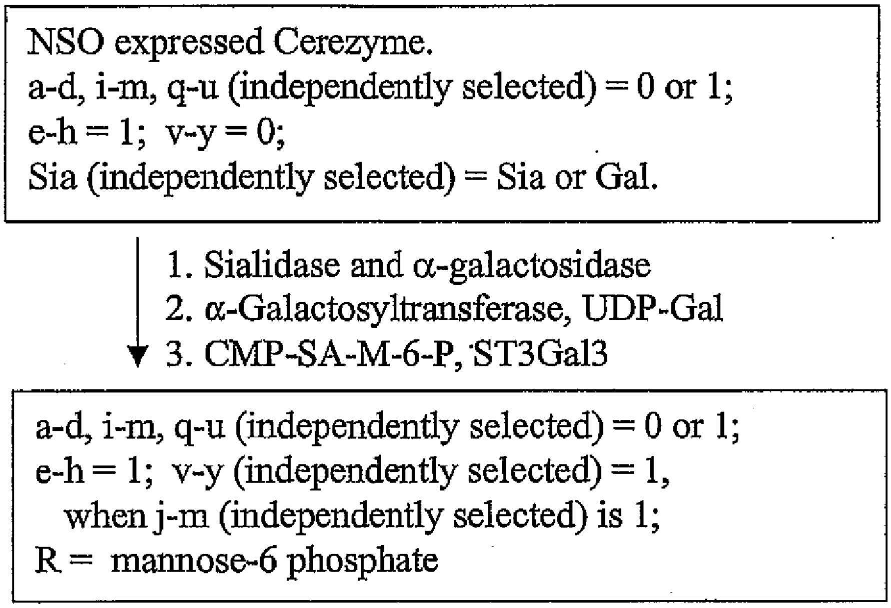


CHO, BHK, 293 cells, Vero expressed Cerezyme.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. Sialidase
2. CMP-SA-M-6-P (1.2 mol eq), ST3Gal3
3. CMP-SA (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = mannose-6-phosphate

FIG. 37C

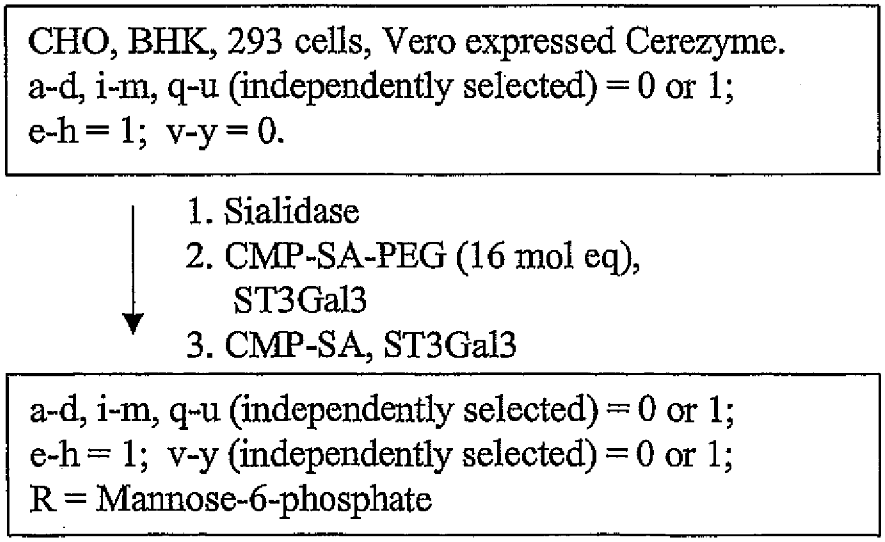


NSO expressed Cerezyme.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0;
Sia (independently selected) = Sia or Gal.

1. Sialidase and α-galactosidase
2. α-Galactosyltransferase, UDP-Gal
3. CMP-SA-M-6-P, ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = mannose-6 phosphate

FIG. 37D



CHO, BHK, 293 cells, Vero expressed Cerezyme.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. Sialidase
2. CMP-SA-PEG (16 mol eq), ST3Gal3
3. CMP-SA, ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = Mannose-6-phosphate

FIG. 37E

CHO, BHK, 293 cells, Vero expressed Cerezyme.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

↓

1. CMP-SA-levulinate, ST3Gal3, buffer, salt
2. H_4N_2-spacer-M-6-P or clustered M-6-P

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = M-6-P or clustered M-6-P

FIG. 37F

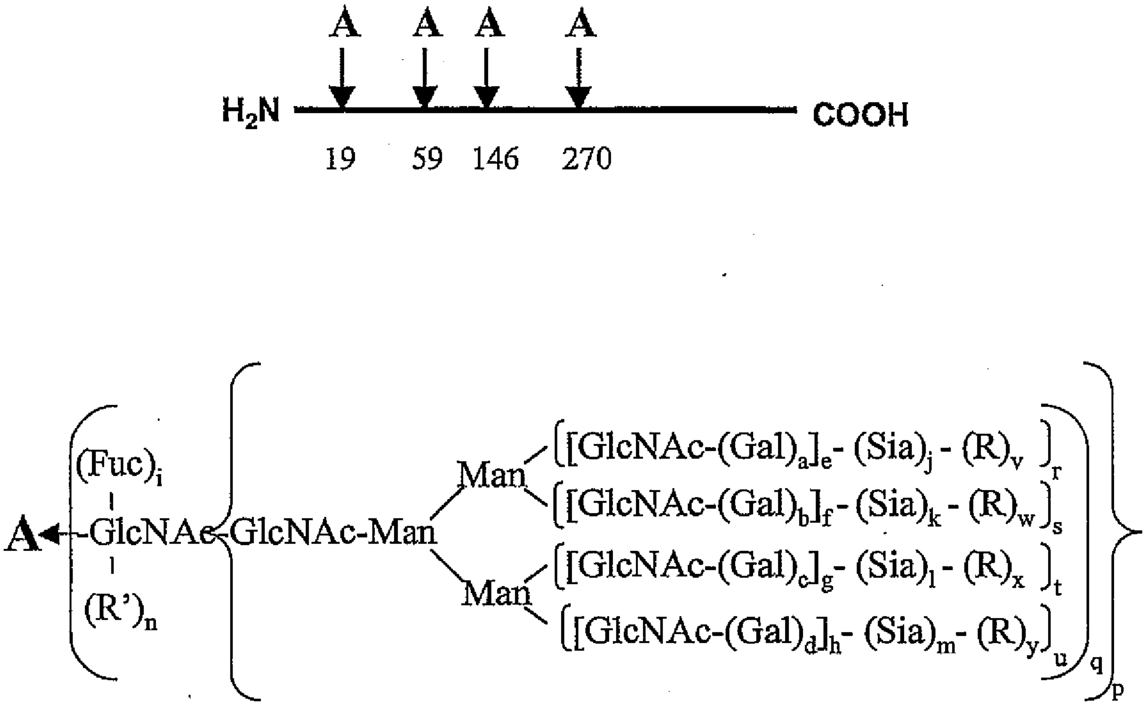
CHO, BHK, 293 cells, Vero expressed Cerezyme.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

↓

1. CMP-SA, α2,8-ST

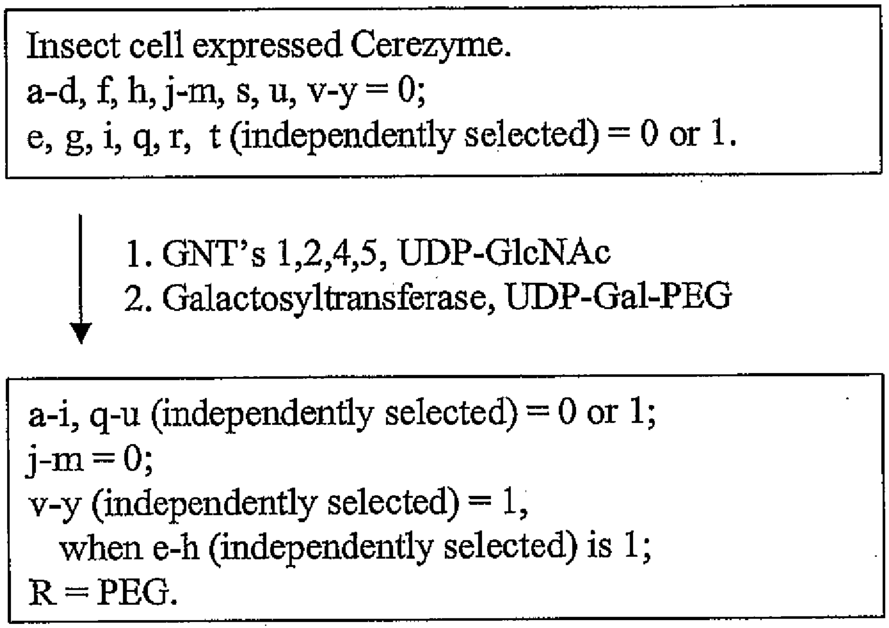
a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1; j-m (independently selected) = 0-20;
v-y (independently selected) = 0.

FIG. 37G


A
A
A
A
H2N
COOH
19
59
146
270
A
(Fuc)i
GlcNAc
(R')n
GlcNAc-Man
Man
Man
[GlcNAc-(Gal)a]e- (Sia)j - (R)v
r
[GlcNAc-(Gal)b]f- (Sia)k - (R)w
s
[GlcNAc-(Gal)c]g- (Sia)l - (R)x
t
[GlcNAc-(Gal)d]h- (Sia)m- (R)y
u
q
p

a-d, i, n, p-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0;
R = modifying group, mannose, oligo-mannose;
R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 37H

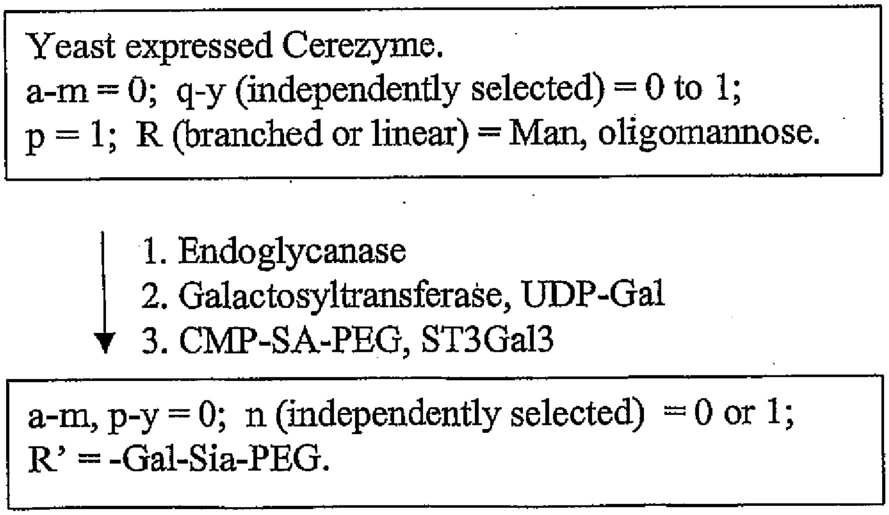


Insect cell expressed Cerezyme.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.

1. GNT's 1,2,4,5, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal-PEG

a-i, q-u (independently selected) = 0 or 1;
j-m = 0;
v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.

FIG. 37I

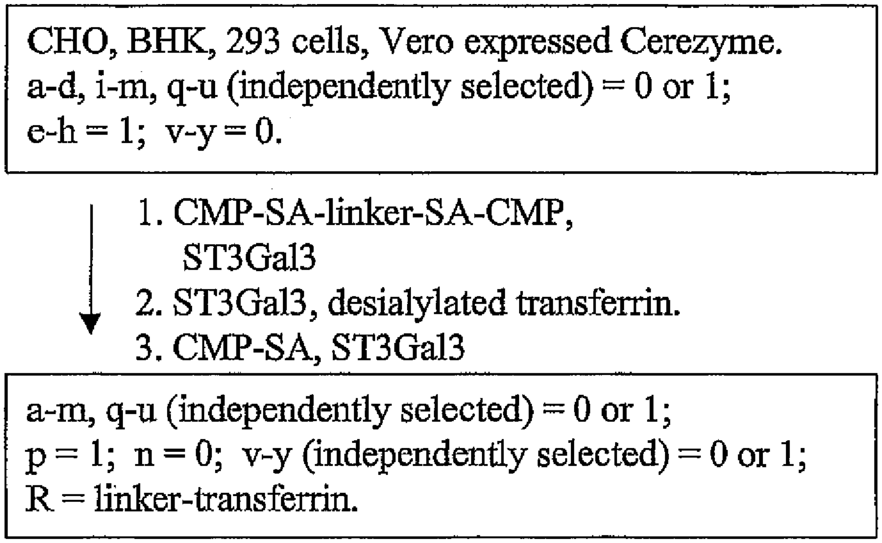


Yeast expressed Cerezyme.
a-m = 0; q-y (independently selected) = 0 to 1;
p = 1; R (branched or linear) = Man, oligomannose.

1. Endoglycanase
2. Galactosyltransferase, UDP-Gal
3. CMP-SA-PEG, ST3Gal3

a-m, p-y = 0; n (independently selected) = 0 or 1;
R' = -Gal-Sia-PEG.

FIG. 37J

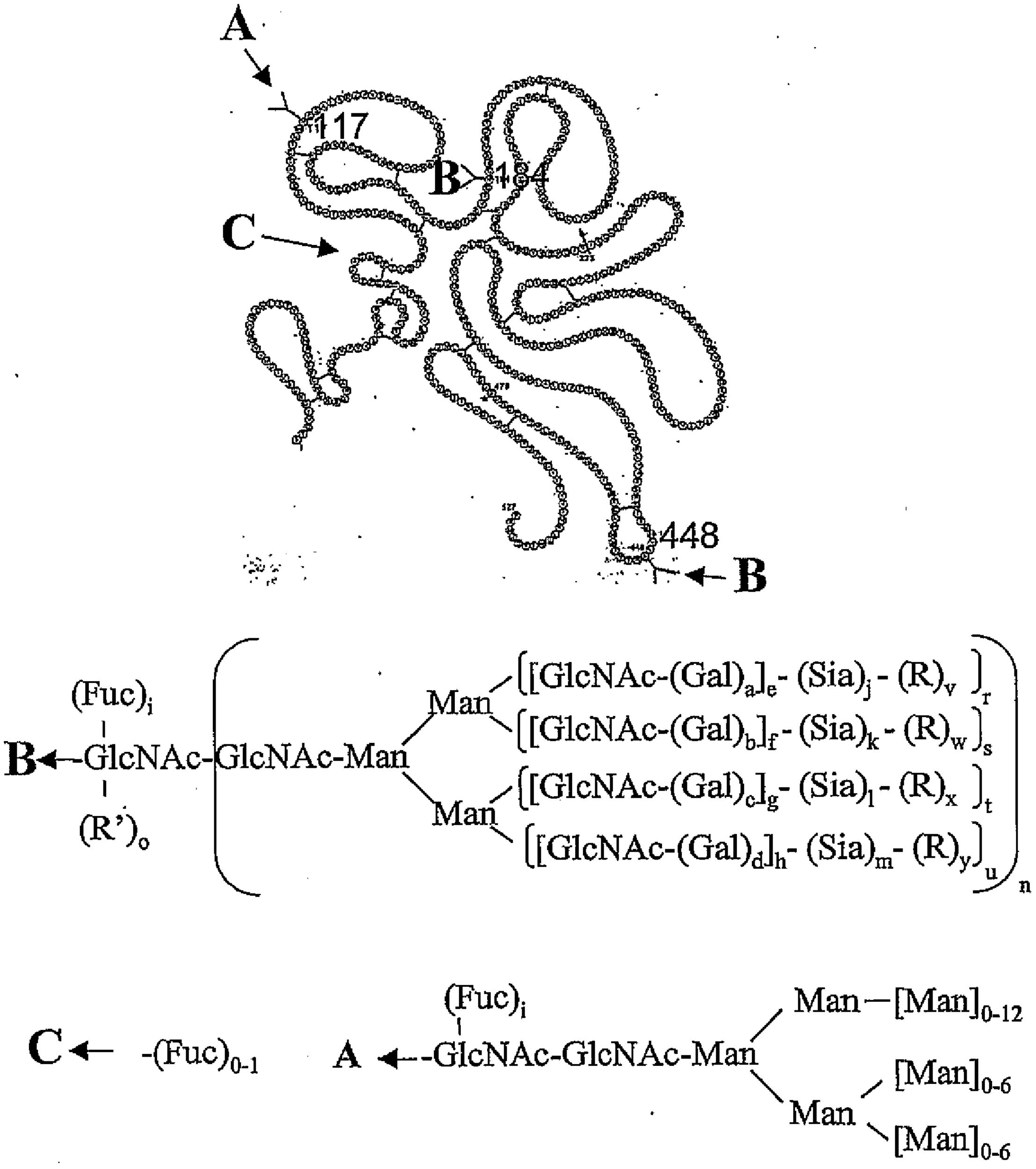


CHO, BHK, 293 cells, Vero expressed Cerezyme.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. CMP-SA-linker-SA-CMP, ST3Gal3
2. ST3Gal3, desialylated transferrin.
3. CMP-SA, ST3Gal3

a-m, q-u (independently selected) = 0 or 1;
p = 1; n = 0; v-y (independently selected) = 0 or 1;
R = linker-transferrin.

FIG. 37K


A
117
B
184
C
448
B
(Fuc)$_i$
B←-GlcNAc-GlcNAc-Man
(R')$_o$
Man
[[GlcNAc-(Gal)$_a$]$_e$- (Sia)$_j$ - (R)$_v$]$_r$
[[GlcNAc-(Gal)$_b$]$_f$- (Sia)$_k$ - (R)$_w$]$_s$
Man
[[GlcNAc-(Gal)$_c$]$_g$- (Sia)$_l$ - (R)$_x$]$_t$
[[GlcNAc-(Gal)$_d$]$_h$- (Sia)$_m$ - (R)$_y$]$_u$
n
C← -(Fuc)$_{0-1}$
(Fuc)$_i$
A ←-GlcNAc-GlcNAc-Man
Man—[Man]$_{0-12}$
Man
[Man]$_{0-6}$
[Man]$_{0-6}$

a-d, i, n-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
j-m (independently selected) = 0 to 20.
R = polymer; R' = sugar, glycoconjugate.

FIG. 38A

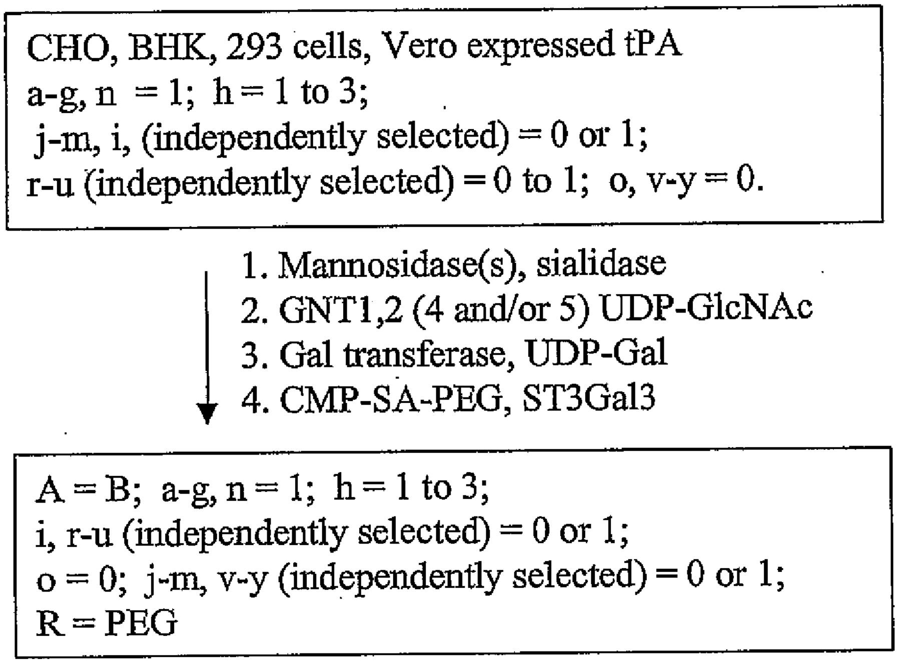

CHO, BHK, 293 cells, Vero expressed tPA
a-g, n = 1; h = 1 to 3;
j-m, i, (independently selected) = 0 or 1;
r-u (independently selected) = 0 to 1; o, v-y = 0.
1. Mannosidase(s), sialidase
2. GNT1,2 (4 and/or 5) UDP-GlcNAc
3. Gal transferase, UDP-Gal
4. CMP-SA-PEG, ST3Gal3
A = B; a-g, n = 1; h = 1 to 3;
i, r-u (independently selected) = 0 or 1;
o = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG

FIG. 38B

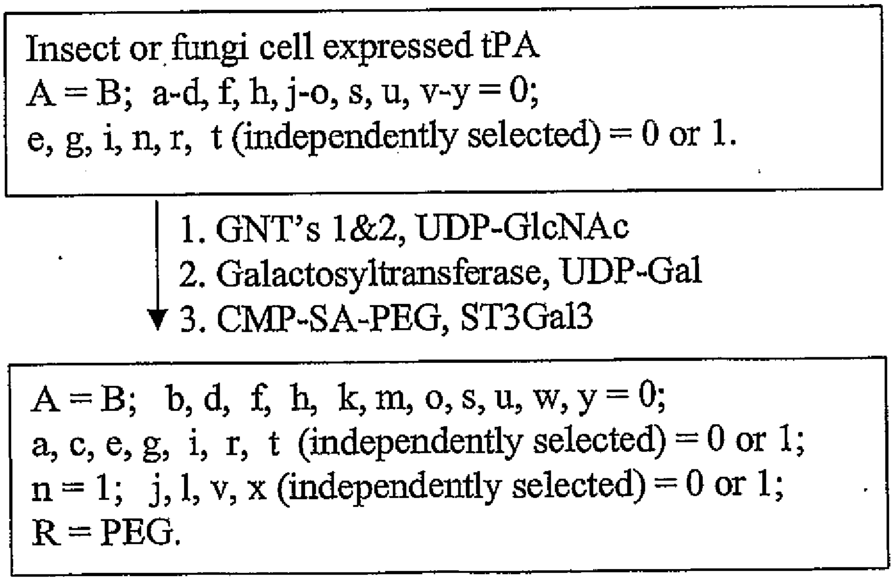

Insect or fungi cell expressed tPA
A = B; a-d, f, h, j-o, s, u, v-y = 0;
e, g, i, n, r, t (independently selected) = 0 or 1.
1. GNT's 1&2, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal
3. CMP-SA-PEG, ST3Gal3
A = B; b, d, f, h, k, m, o, s, u, w, y = 0;
a, c, e, g, i, r, t (independently selected) = 0 or 1;
n = 1; j, l, v, x (independently selected) = 0 or 1;
R = PEG.

FIG. 38C

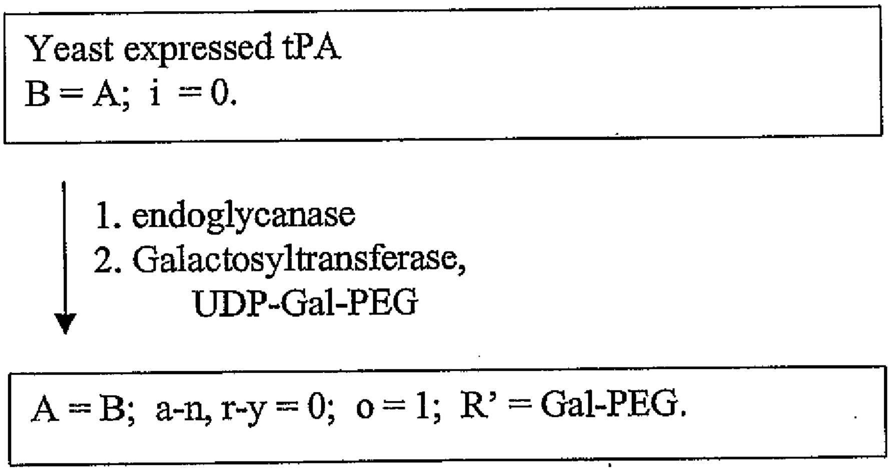

Yeast expressed tPA
B = A; i = 0.
1. endoglycanase
2. Galactosyltransferase,
UDP-Gal-PEG
A = B; a-n, r-y = 0; o = 1; R' = Gal-PEG.

FIG. 38D

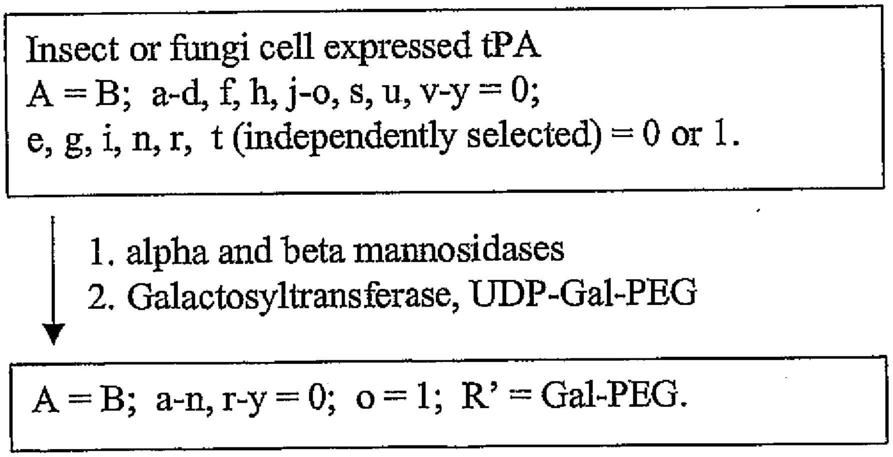

Insect or fungi cell expressed tPA
A = B; a-d, f, h, j-o, s, u, v-y = 0;
e, g, i, n, r, t (independently selected) = 0 or 1.
1. alpha and beta mannosidases
2. Galactosyltransferase, UDP-Gal-PEG
A = B; a-n, r-y = 0; o = 1; R' = Gal-PEG.

FIG. 38E

Insect or fungi cell expressed tPA
A = B; a-d, f, h, j-o, s, u, v-y = 0;
e, g, i, n, r, t (independently selected) = 0 or 1.

1. GNT's 1&2, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal-PEG

A = B; b, d, f, h, j-o, s, u, w, y = 0;
a, c, e, g, i, r, t, v, x (independently selected)= 0 or 1;
n = 1; R = PEG.

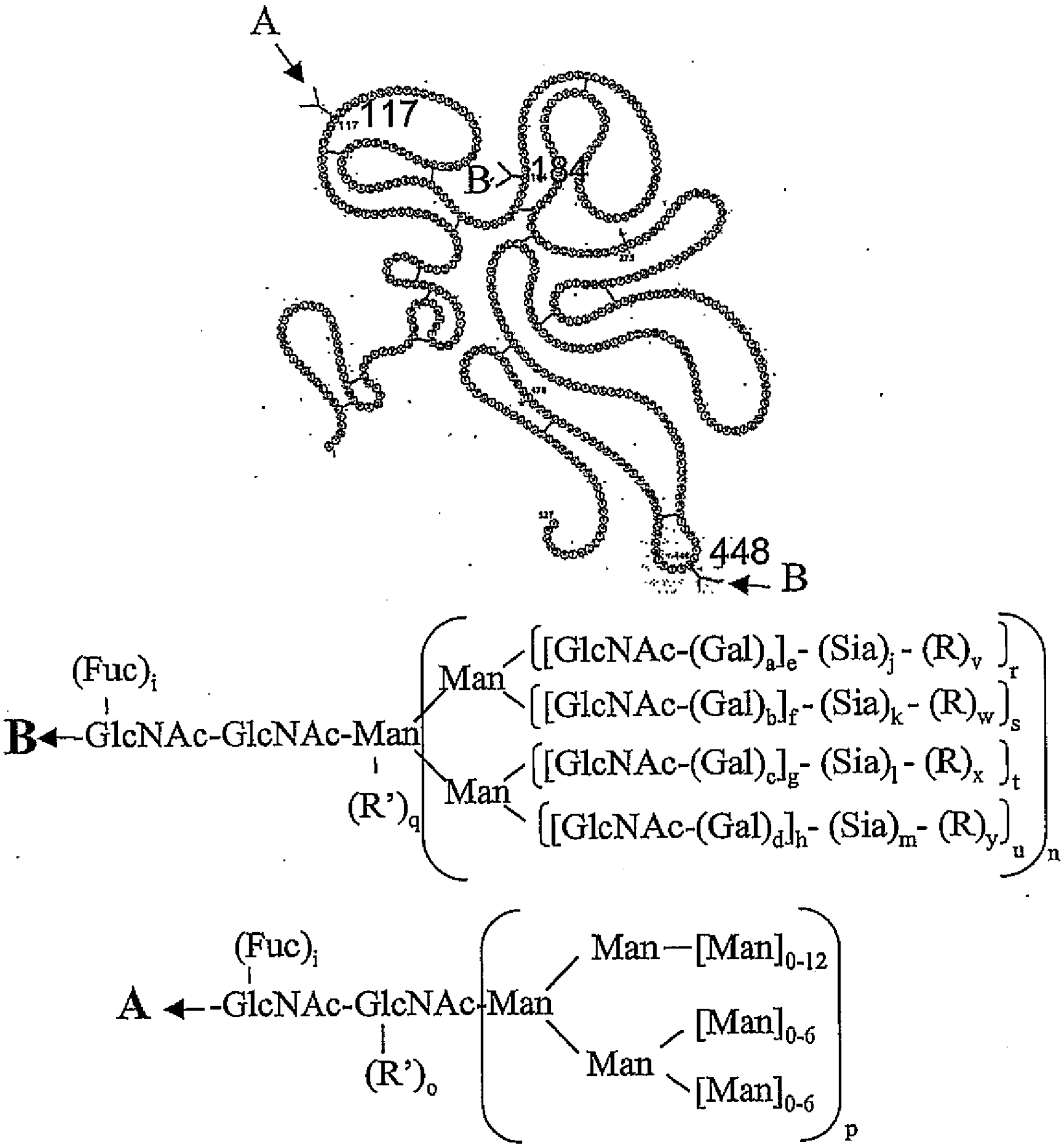
FIG. 38F

Insect or fungi cell expressed tPA
A = B; a-d, f, h, j-o, s, u, v-y = 0;
e, g, i, n, r, t (independently selected) = 0 or 1.

1. GNT's 1 & 2, UDP-GlcNAc
2. Galactosidase (synthetic enzyme), PEG-Gal-F.

A = B; b, d, f, h, j-o, s, u, w, y = 0;
a, c, e, g, i, r, t, v, x (independently selected)= 0 or 1;
n = 1; R = PEG.

FIG. 38G


A
117
B
184
448
B
(Fuc)i
B←-GlcNAc-GlcNAc-Man
(R')q
Man
[[GlcNAc-(Gal)a]e-(Sia)j-(R)v]r
[[GlcNAc-(Gal)b]f-(Sia)k-(R)w]s
Man
[[GlcNAc-(Gal)c]g-(Sia)l-(R)x]t
[[GlcNAc-(Gal)d]h-(Sia)m-(R)y]u
n
(Fuc)i
A ←-GlcNAc-GlcNAc-Man
(R')o
Man—[Man]0-12
Man
[Man]0-6
[Man]0-6
p

a-d, i, n-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
j-m (independently selected) = 0 to 20.
R = polymer; R' = sugar, glycoconjugate.

FIG. 38H

NSO expressed tPA
A = B; a-m, r-u (independently selected) = 0 or 1;
n = 1; o, p, q, v-y = 0

↓
1. sialidase, alpha-galactosidase
2. CMP-SA-levulinate, ST3Gal3,
3. H_4N_2-PEG

A = B; a-m, r-y (independently selected) = 0 or 1;
n = 1; o, p, q = 0;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.

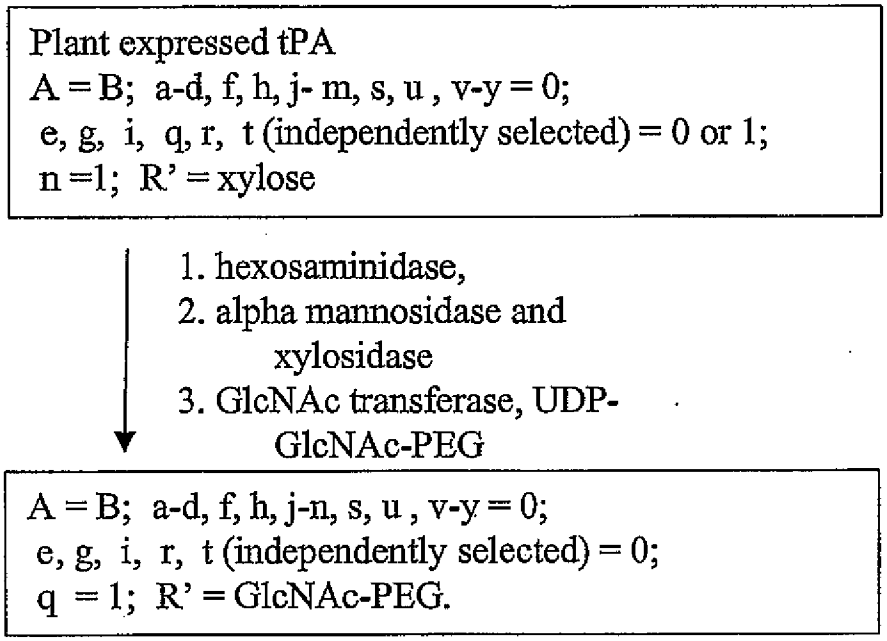
FIG. 38I

CHO, BHK, 293 cells, Vero expressed tPA
a-g, n, p = 1; h = 1 to 3;
j-m, i, (independently selected) = 0 or 1;
r-u (independently selected) = 0 to 1; q, o, v-y = 0.

↓
1. alpha and beta Mannosidases
2. CMP-SA, ST3Gal3
3. Galactosyltransferase, UDP-Gal-PEG

a-g, n = 1; h = 1 to 3;
i, r-u (independently selected) = 0 or 1; o = 1;
q, p, v-y = 0; j-m (independently selected) = 0 or 1;
R' = Gal-PEG

FIG. 38J

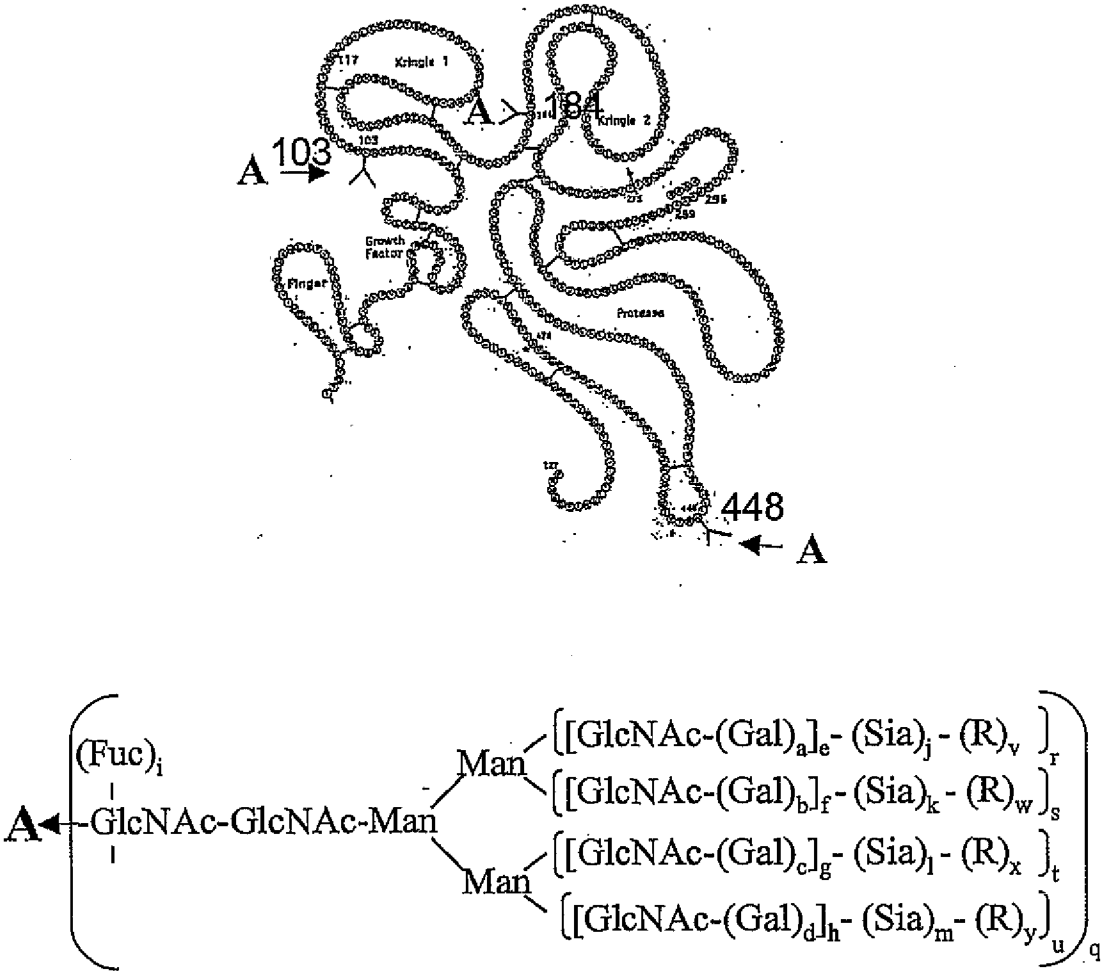


Plant expressed tPA
A = B; a-d, f, h, j- m, s, u , v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1;
n =1; R' = xylose

1. hexosaminidase,
2. alpha mannosidase and xylosidase
3. GlcNAc transferase, UDP-GlcNAc-PEG

A = B; a-d, f, h, j-n, s, u , v-y = 0;
e, g, i, r, t (independently selected) = 0;
q = 1; R' = GlcNAc-PEG.

FIG. 38K


117
Kringle 1
A
184
Kringle 2
A
103
103
Growth Factor
Finger
296
Protease
448
A
(Fuc)i
A
GlcNAc-GlcNAc-Man
Man
Man
[[GlcNAc-(Gal)a]e- (Sia)j - (R)v]r
[[GlcNAc-(Gal)b]f- (Sia)k - (R)w]s
[[GlcNAc-(Gal)c]g- (Sia)l - (R)x]t
[[GlcNAc-(Gal)d]h- (Sia)m- (R)y]u
q

a-d, i, q-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0; R = polymer.

FIG. 38L

CHO, BHK, 293 cells, Vero expressed TNK tPA
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. Sialidase
2. CMP-SA-PEG (16 mol eq), ST3Gal3

↓

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.

FIG. 38M

CHO, BHK, 293 cells, Vero expressed TNK tPA
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. Sialidase
2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
3. CMP-SA (16 mol eq), ST3Gal3

↓

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 38N

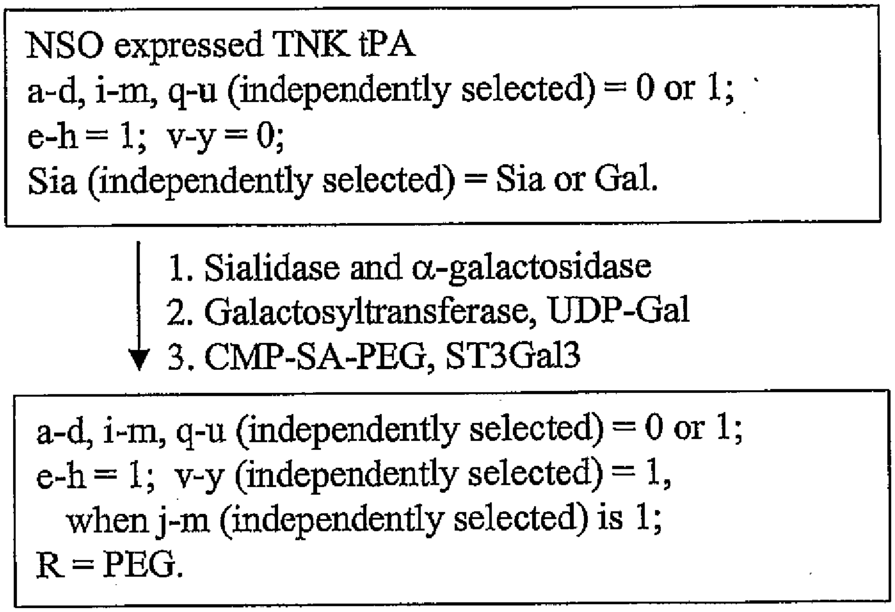
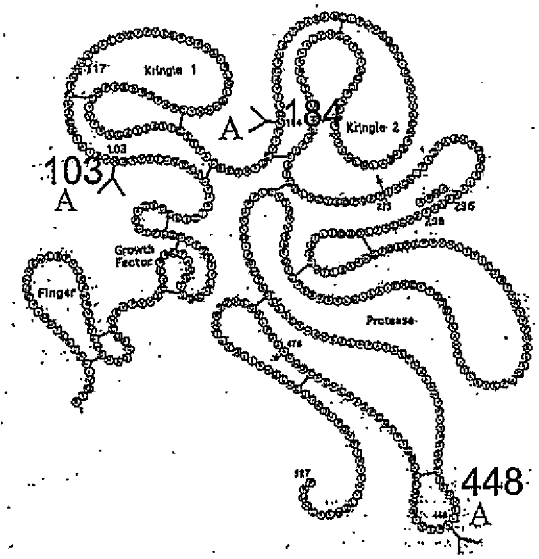
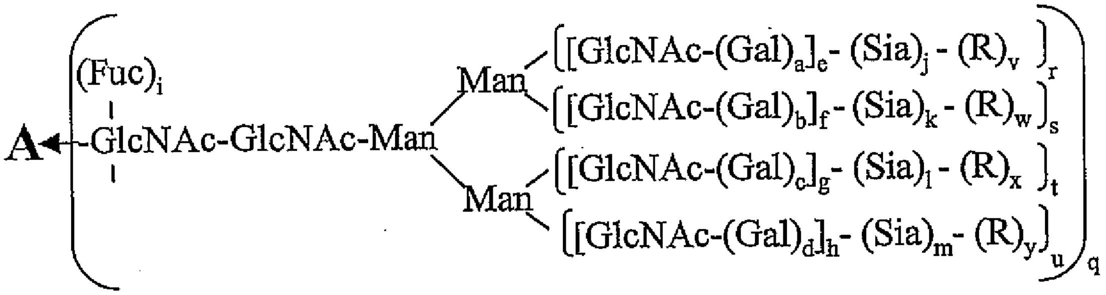

NSO expressed TNK tPA
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0;
Sia (independently selected) = Sia or Gal.
1. Sialidase and α-galactosidase
2. Galactosyltransferase, UDP-Gal
3. CMP-SA-PEG, ST3Gal3
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.

FIG. 38O




A
(Fuc)$_i$
-GlcNAc-GlcNAc-Man
Man
Man
[[GlcNAc-(Gal)$_a$]$_e$- (Sia)$_j$ - (R)$_v$]$_r$
[[GlcNAc-(Gal)$_b$]$_f$- (Sia)$_k$ - (R)$_w$]$_s$
[[GlcNAc-(Gal)$_c$]$_g$- (Sia)$_l$ - (R)$_x$]$_t$
[[GlcNAc-(Gal)$_d$]$_h$- (Sia)$_m$- (R)$_y$]$_u$
q

a-d, i, q-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0; R = polymer.

FIG. 38P

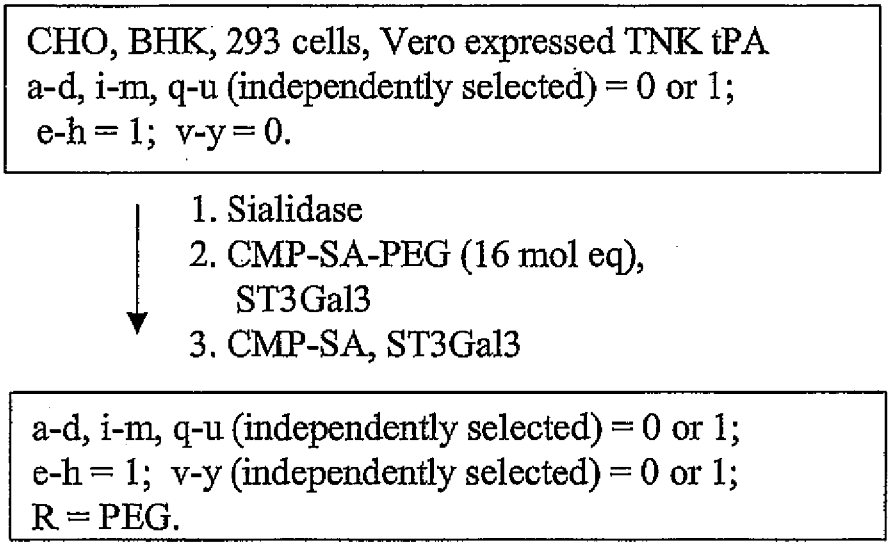

CHO, BHK, 293 cells, Vero expressed TNK tPA
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
1. Sialidase
2. CMP-SA-PEG (16 mol eq), ST3Gal3
3. CMP-SA, ST3Gal3
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 38Q

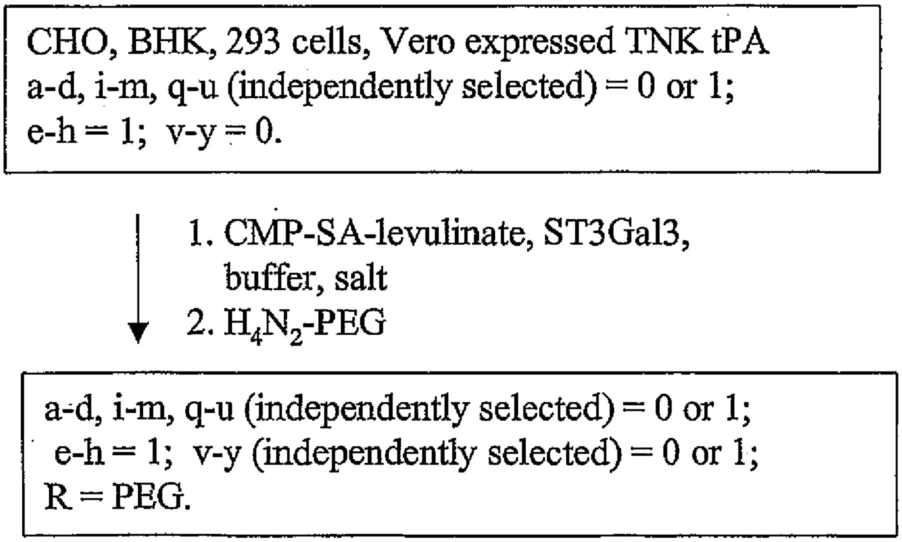

CHO, BHK, 293 cells, Vero expressed TNK tPA
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
1. CMP-SA-levulinate, ST3Gal3, buffer, salt
2. H4N2-PEG
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 38R

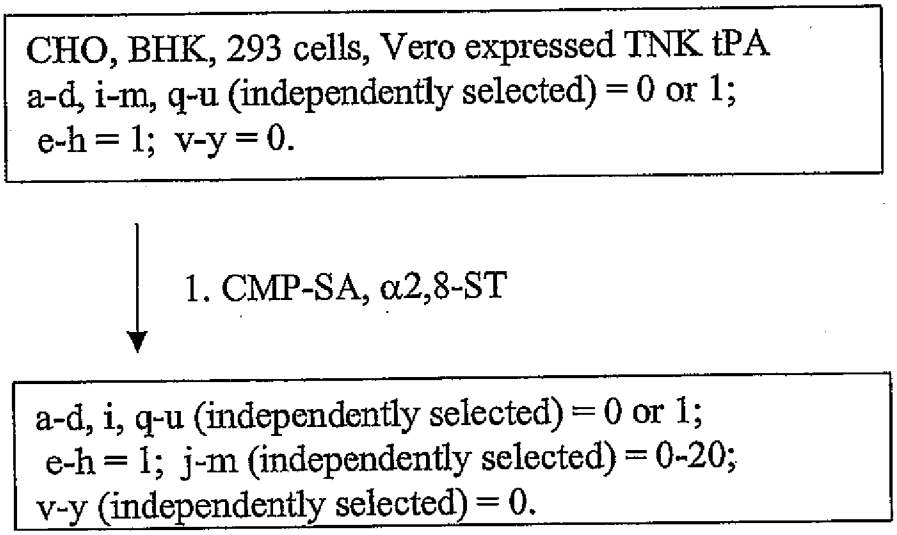
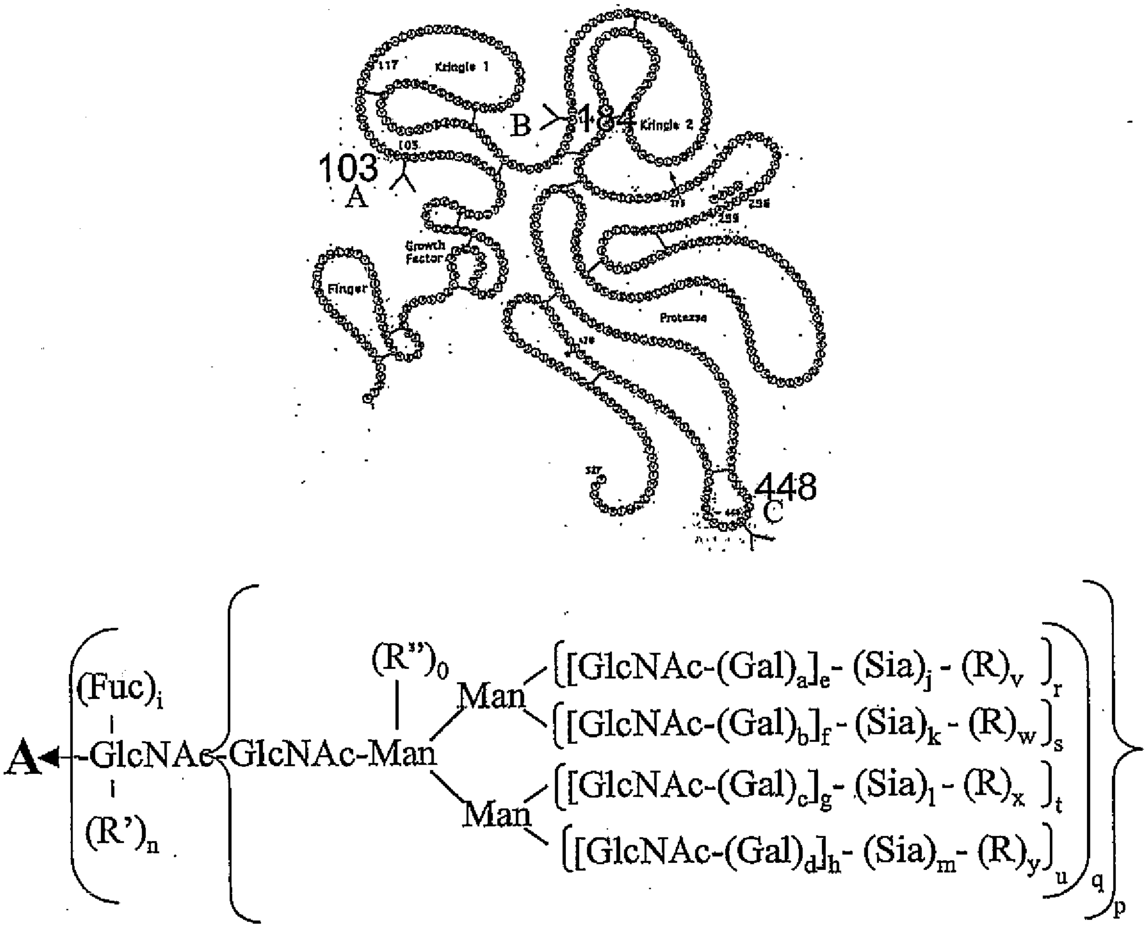

CHO, BHK, 293 cells, Vero expressed TNK tPA
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
1. CMP-SA, α2,8-ST
a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1; j-m (independently selected) = 0-20;
v-y (independently selected) = 0.

FIG. 38S


117
Kringle 1
B
184
Kringle 2
103
105
A
Growth Factor
Finger
Protease
448
C
A
(Fuc)i
GlcNAc
GlcNAc-Man
(R')n
(R'')0
Man
Man
[[GlcNAc-(Gal)a]e- (Sia)j - (R)v]r
[[GlcNAc-(Gal)b]f - (Sia)k - (R)w]s
[[GlcNAc-(Gal)c]g- (Sia)l - (R)x]t
[[GlcNAc-(Gal)d]h- (Sia)m- (R)y]u
q
p

a-d, i, n-y (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
R = modifying group, mannose, oligo-mannose;
R' = H, glycosyl residue, modifying group, glycoconjugate.
R'' = glycosyl residue.

FIG. 38T

Insect cell expressed TNK tPA
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.

↓
1. GNT's 1,2,4,5, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal-PEG

a-i, q-u (independently selected) = 0 or 1;
j-m = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.

FIG. 38U

Yeast expressed TNK tPA
a-m = 0; q-y (independently selected) = 0 to 1; p = 1;
R (branched or linear) = Man, oligomannose.

↓
1. Endoglycanase
2. Galactosyltransferase, UDP-Gal-PEG

a-m, p-y = 0; n (independently selected) = 0 or 1;
R' = -Gal-PEG.

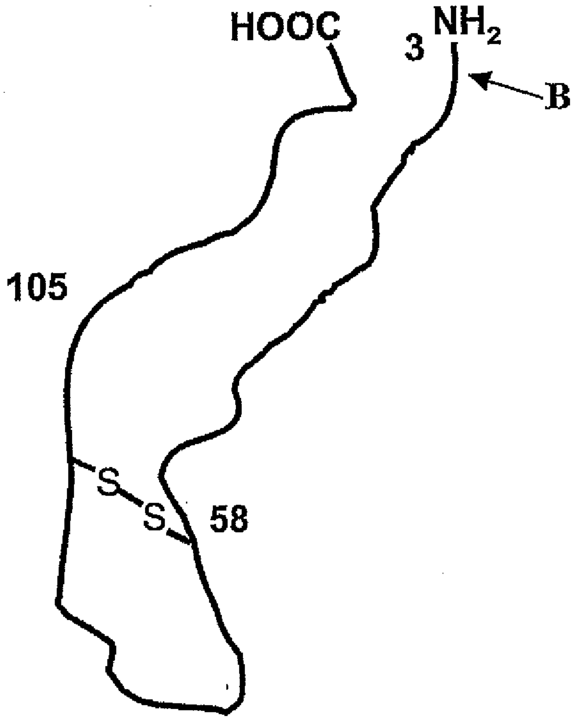
FIG. 38V

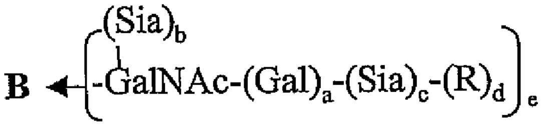
CHO, BHK, 293 cells, Vero expressed TNK tPA
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. CMP-SA-linker-Gal-UDP, ST3Gal3
2. Galactosyltransferase, anti-TNF IG chimera produced in CHO.

a-m, r-u (independently selected) = 0 or 1; p, q = 1;
n = 0; v-y (independently selected) = 0 or 1;
R = linker-anti-TNF IG chimera protein.

FIG. 38W





$$B \leftarrow \left[-\overset{(\mathrm{Sia})_b}{\mathrm{GalNAc}}-(\mathrm{Gal})_a-(\mathrm{Sia})_c-(\mathrm{R})_d \right]_e$$

a-c, e (independently selected) = 0 or 1;
d = 0;
R = modifying group, mannose, oligomannose.

FIG. 39A

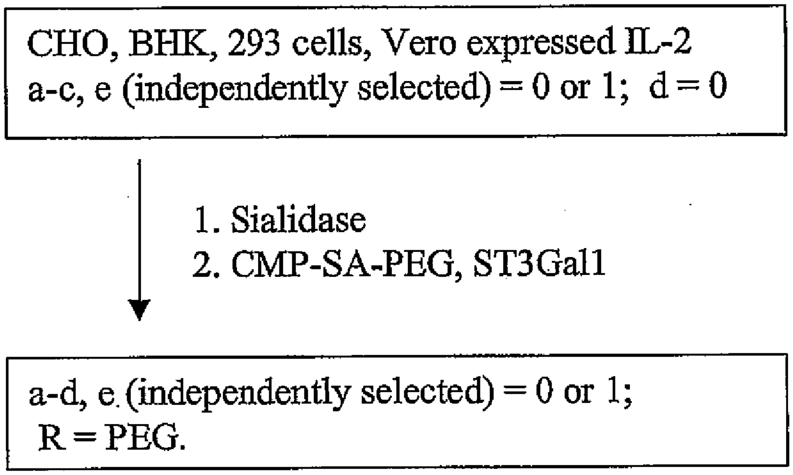

CHO, BHK, 293 cells, Vero expressed IL-2
a-c, e (independently selected) = 0 or 1; d = 0
1. Sialidase
2. CMP-SA-PEG, ST3Gal1
a-d, e (independently selected) = 0 or 1;
R = PEG.

FIG. 39B

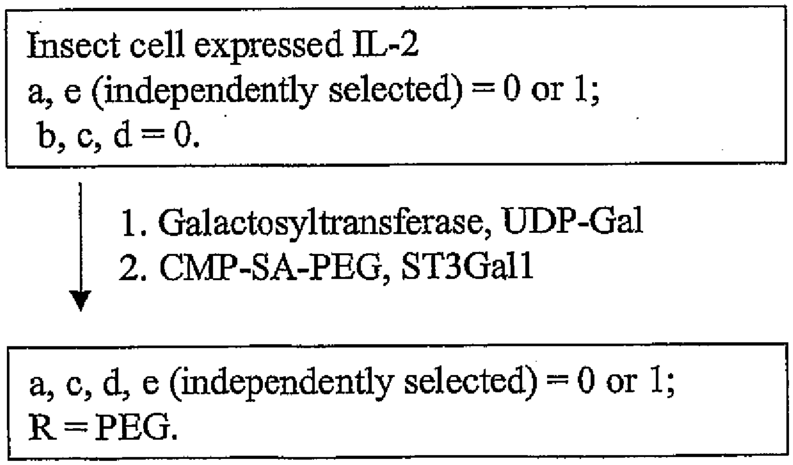

Insect cell expressed IL-2
a, e (independently selected) = 0 or 1;
b, c, d = 0.
1. Galactosyltransferase, UDP-Gal
2. CMP-SA-PEG, ST3Gal1
a, c, d, e (independently selected) = 0 or 1;
R = PEG.

FIG. 39C

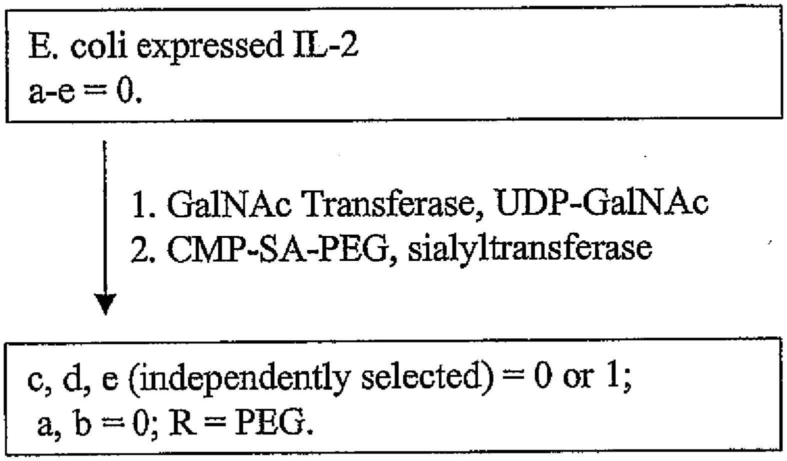

E. coli expressed IL-2
a-e = 0.
1. GalNAc Transferase, UDP-GalNAc
2. CMP-SA-PEG, sialyltransferase
c, d, e (independently selected) = 0 or 1;
a, b = 0; R = PEG.

FIG. 39D

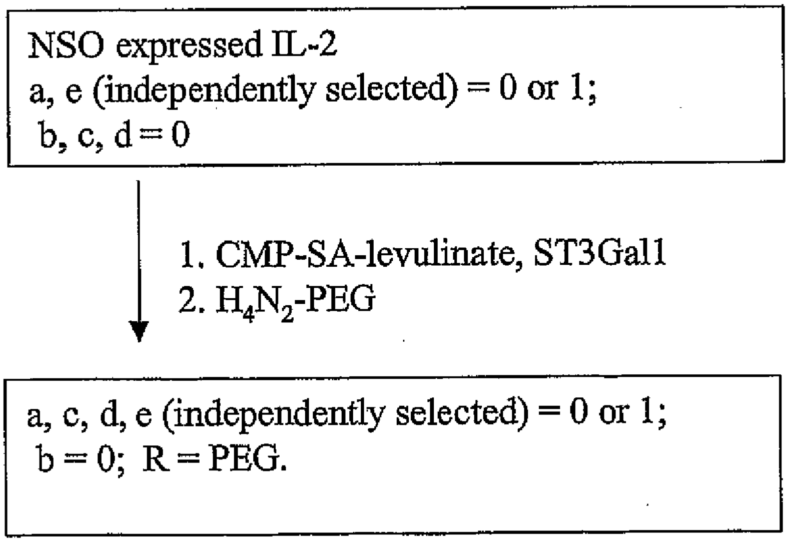

NSO expressed IL-2
a, e (independently selected) = 0 or 1;
b, c, d = 0
1. CMP-SA-levulinate, ST3Gal1
2. H_4N_2-PEG
a, c, d, e (independently selected) = 0 or 1;
b = 0; R = PEG.

FIG. 39E

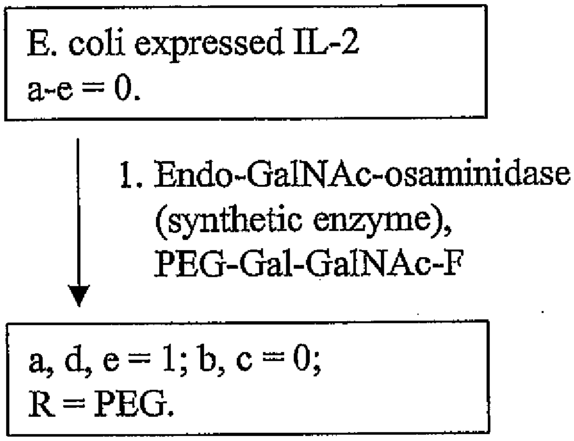


FIG. 39F

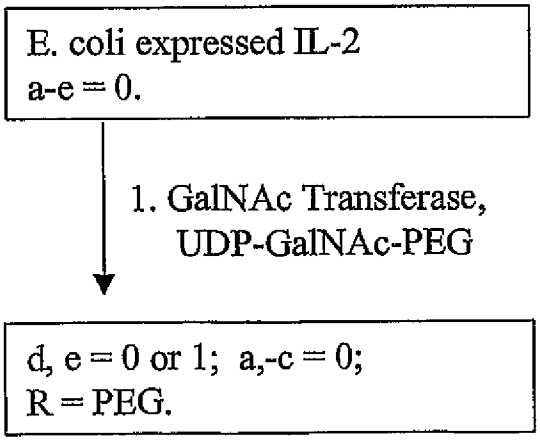
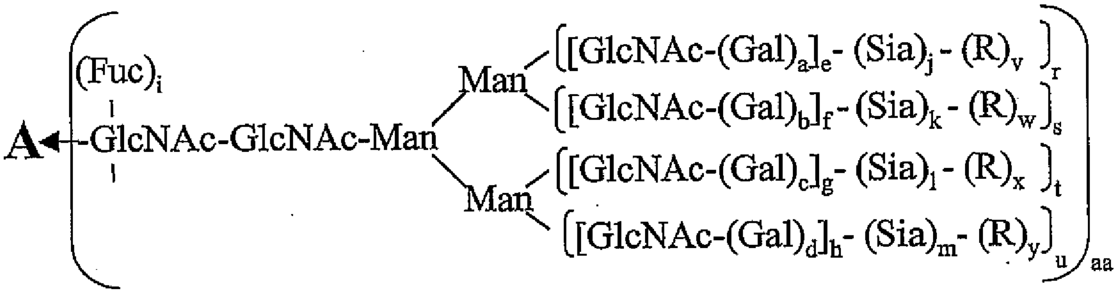
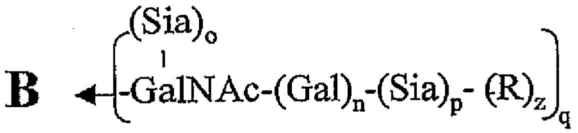


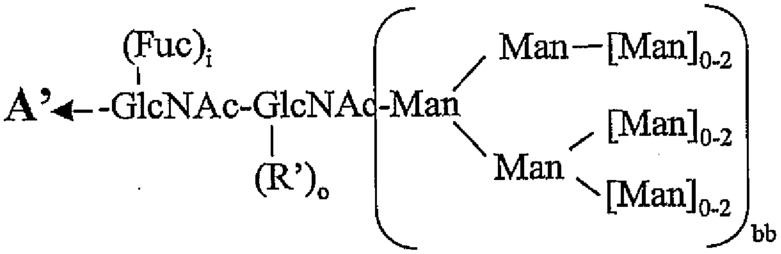
FIG. 39G

2 peptides
A and A' - N-linked sites
B - O-linked sites


A
(Fuc)i
-GlcNAc-GlcNAc-Man
Man
Man
[[GlcNAc-(Gal)a]e- (Sia)j - (R)v]r
[[GlcNAc-(Gal)b]f - (Sia)k - (R)w]s
[[GlcNAc-(Gal)c]g- (Sia)l - (R)x]t
[[GlcNAc-(Gal)d]h- (Sia)m- (R)y]u
aa



$$\mathbf{B} \leftarrow \left[\overset{(\mathrm{Sia})_o}{\mathrm{-GalNAc}}\mathrm{-(Gal)_n-(Sia)_p-(R)_z} \right]_q$$



Alternate structure for some N-linked structures of A.

a-d, i, n-u (independently selected) = 0 or 1.
aa, bb (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 20.
v-z = 0; R = polymer, glycoconjugate.

FIG. 40A

CHO, BHK, 293s cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, a-d, j-m, i, n-u (independently selected) = 0 or 1;
v-z = 0.

1. Sialidase
2. CMP-SA-PEG, ST3Gal3

e-h = 1 to 4;
aa, bb, a-d, i, n, q-u (independently selected) = 0 or 1;
o, p, z = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 40B

CHO, BHK, 293S cells, Vero, MDCK, 293S, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, a-d, j-m, i, n-u (independently selected) = 0 or 1;
v-z = 0.

1. Sialidase
2. CMP-SA-PEG, ST3Gal3
3. ST3Gal1, CMP-SA

e-h = 1 to 4;
aa, bb, a-d, i, n, p-u (independently selected) = 0 or 1;
o, z = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 40C

CHO, BHK, 293s cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, a-d, j-m, i, n-u (independently selected)=0 or 1;
v-z = 0.

↓ 1. CMP-SA-PEG, ST3Gal3

e-h = 1 to 4;
aa, bb, a-d, i, n-u (independently selected) = 0 or 1;
z = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 40D

CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, a-d, j-m, i, n-u (independently selected) 0 or 1;
v-z = 0.

↓ 1. CMP-SA-PEG, ST3Gal1

e-h = 1 to 4;
aa, bb, a-d, i, n-u (independently selected) = 0 or 1;
z = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 40E

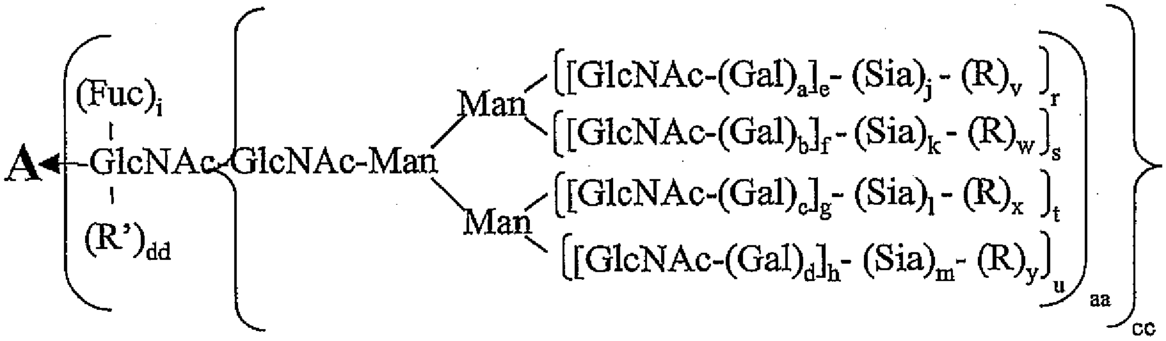
CHO, BHK, 293S cells, Vero, MDCK, HEKC
expressed Factor VIII.
e-h = 1 to 4;
aa, bb, a-d, j-m, i, n-u (independently selected)=0 or 1;
v-z = 0.

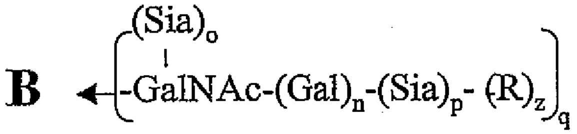
$\downarrow$ 1. CMP-SA-PEG, α2,8-ST

e-h = 1 to 4;
aa, bb, a-d, i, n-y (independently selected) = 0 or 1;
z = 0; j-m (independently selected) = 0 to 2;
v-y (independently selected) = 1,
when j-m (independently selected) is 2;
R = PEG.

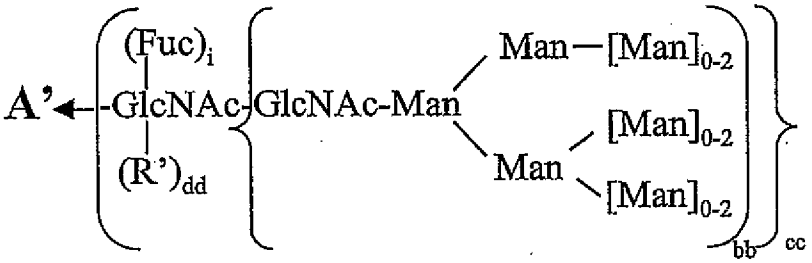
FIG. 40F

2 peptides
A or A' - N-linked sites
B - O-linked sites


A
(Fuc)i
-GlcNAc-GlcNAc-Man
(R')dd
Man
[[GlcNAc-(Gal)a]e- (Sia)j - (R)v]r
[[GlcNAc-(Gal)b]f - (Sia)k - (R)w]s
Man
[[GlcNAc-(Gal)c]g- (Sia)l - (R)x]t
[[GlcNAc-(Gal)d]h- (Sia)m- (R)y]u
aa
cc



$$\mathbf{B} \leftarrow \left[\text{-}\overset{(\text{Sia})_o}{\text{GalNAc}}\text{-}(\text{Gal})_n\text{-}(\text{Sia})_p\text{-}(\text{R})_z\right]_q$$



Alternate structure for some N-linked structures of A.

a-d, i, n-u, (independently selected) = 0 or 1.
aa, bb, cc, dd (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 20.
v-z = 0;
R = modifying group, mannose, oligo-mannose.
R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 40G

CHO, BHK, 293S cells, Vero, MDCK, HEKC
expressed Factor VIII.
e-h = 1 to 4;
aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;
dd, v-z = 0.

1. CMP-SA-levulinate, ST3Gal3,
2. H_4N_2-PEG

e-h = 1 to 4;
aa, bb, cc, a-d, i, n-u (independently selected) = 0 or 1;
dd, z = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 40H

CHO, BHK, 293S cells, Vero, MDCK, HEKC
expressed Factor VIII.
e-h = 1 to 4;
aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;
dd, v-z = 0.

1. endo-H
2. galactosyltransferase, UDP-Gal-PEG

e-h = 1 to 4;
aa, bb, dd, a-d, i, j-u (independently selected) = 0 or 1;
cc, v-z = 0; R' = -Gal-PEG.

FIG. 40I

CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;
dd, v-z = 0.

↓
1. ST3Gal3, CMP-SA
2. endo-H
3. galactosyltransferase, UDP-Gal-PEG

e-h = 1 to 4;
aa, bb, dd, a-d, i, j-u (independently selected) = 0 or 1;
cc, v-z = 0; R' = -Gal-PEG.

FIG. 40J

CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;
dd, v-z = 0.

↓
1. mannosidases
2. GNT 1 & 2, UDP-GlcNAc
3. galactosyltransferase, UDP-Gal-PEG

e-h = 1 to 4;
aa, a-d, i, j-y (independently selected) = 0 or 1;
bb, cc, dd, z = 0; R = PEG.

FIG. 40K

CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;
dd, v-z = 0.

↓
1. mannosidases
2. GNT-1,2, 4 & 5; UDP-GlcNAc
3. galactosyltransferase, UDP-Gal
4. ST3Gal3, CMP-SA

e-h = 1 to 4;
aa, bb, cc, a-d, i, j-q (independently selected) = 0 or 1;
dd, v-z = 0.

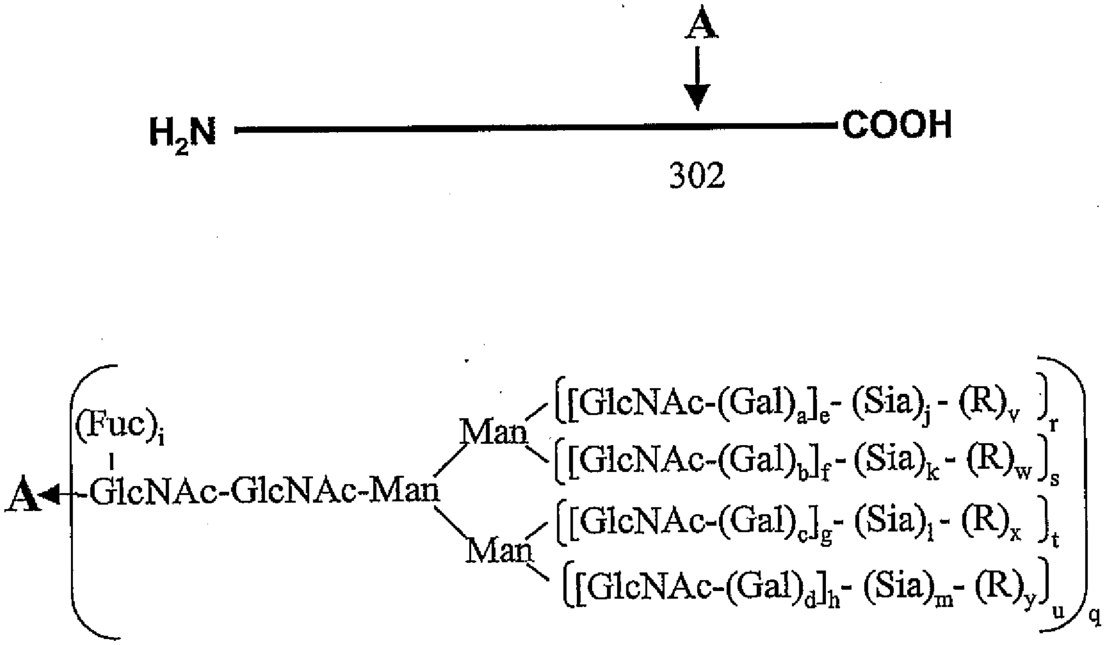
FIG. 40L

CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;
dd, v-z = 0.

↓
1. mannosidases
2. GNT-1, UDP-GlcNAc-PEG

e-h = 0 to 4;
aa, a-d, i, j-y (independently selected) = 0 or 1;
bb, cc, dd, z = 0.

FIG. 40M


A
H2N
COOH
302
(Fuc)i
A
GlcNAc-GlcNAc-Man
Man
Man
[[GlcNAc-(Gal)a]e- (Sia)j - (R)v]r
[[GlcNAc-(Gal)b]f - (Sia)k - (R)w]s
[[GlcNAc-(Gal)c]g- (Sia)l - (R)x]t
[[GlcNAc-(Gal)d]h- (Sia)m- (R)y]u
q

a-d, i, q-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0; R = polymer.

FIG. 41A

CHO, BHK, 293 cells, Vero expressed Urokinase.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

↓
1. Sialidase
2. CMP-SA-PEG (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.

FIG. 41B

CHO, BHK, 293 cells, Vero expressed Urokinase.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

↓
1. Sialidase
2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
3. CMP-SA (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 41C

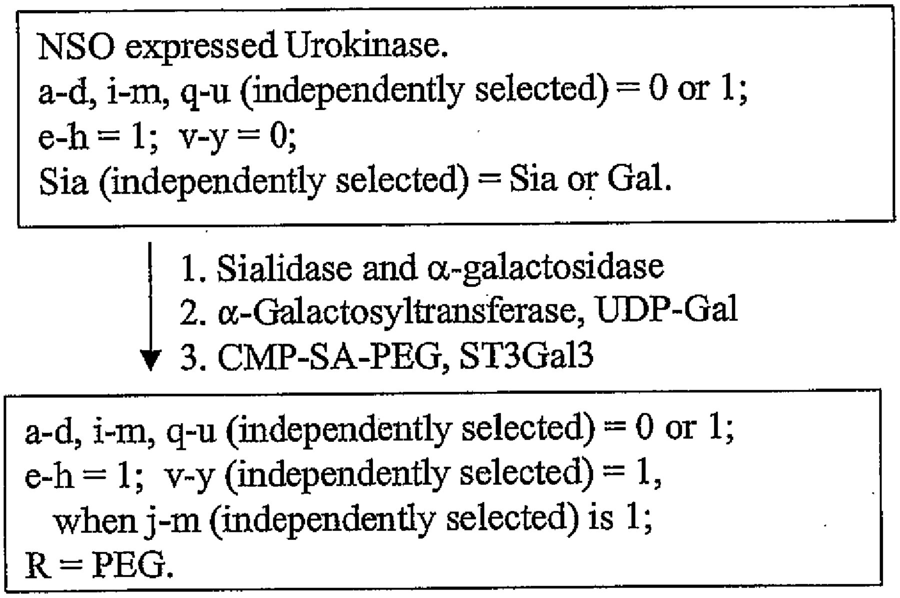

NSO expressed Urokinase.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0;
Sia (independently selected) = Sia or Gal.
1. Sialidase and α-galactosidase
2. α-Galactosyltransferase, UDP-Gal
3. CMP-SA-PEG, ST3Gal3
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.

FIG. 41D

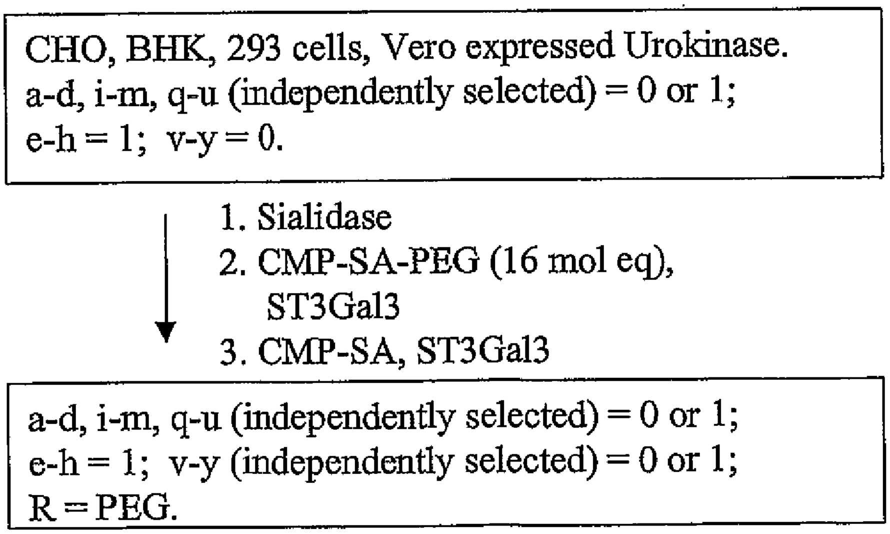
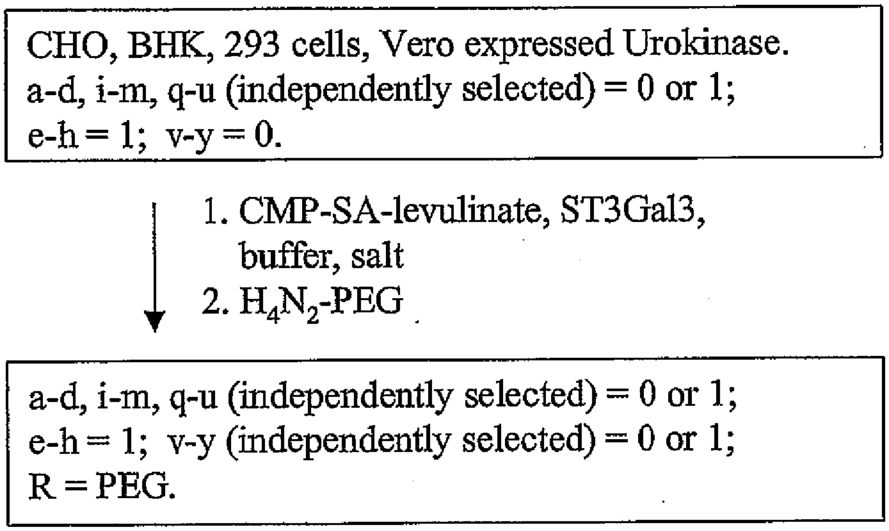

CHO, BHK, 293 cells, Vero expressed Urokinase.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
1. Sialidase
2. CMP-SA-PEG (16 mol eq),
ST3Gal3
3. CMP-SA, ST3Gal3
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 41E

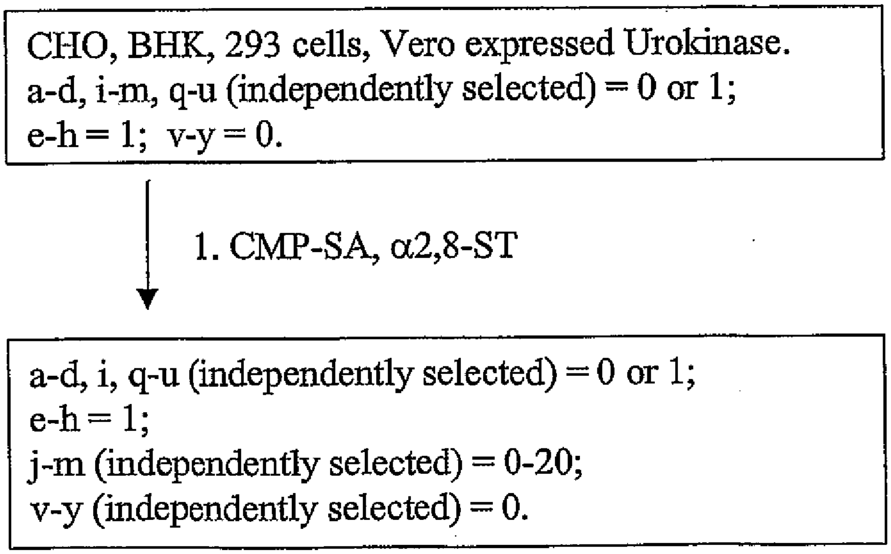


CHO, BHK, 293 cells, Vero expressed Urokinase.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. CMP-SA-levulinate, ST3Gal3, buffer, salt
2. H_4N_2-PEG

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 41F

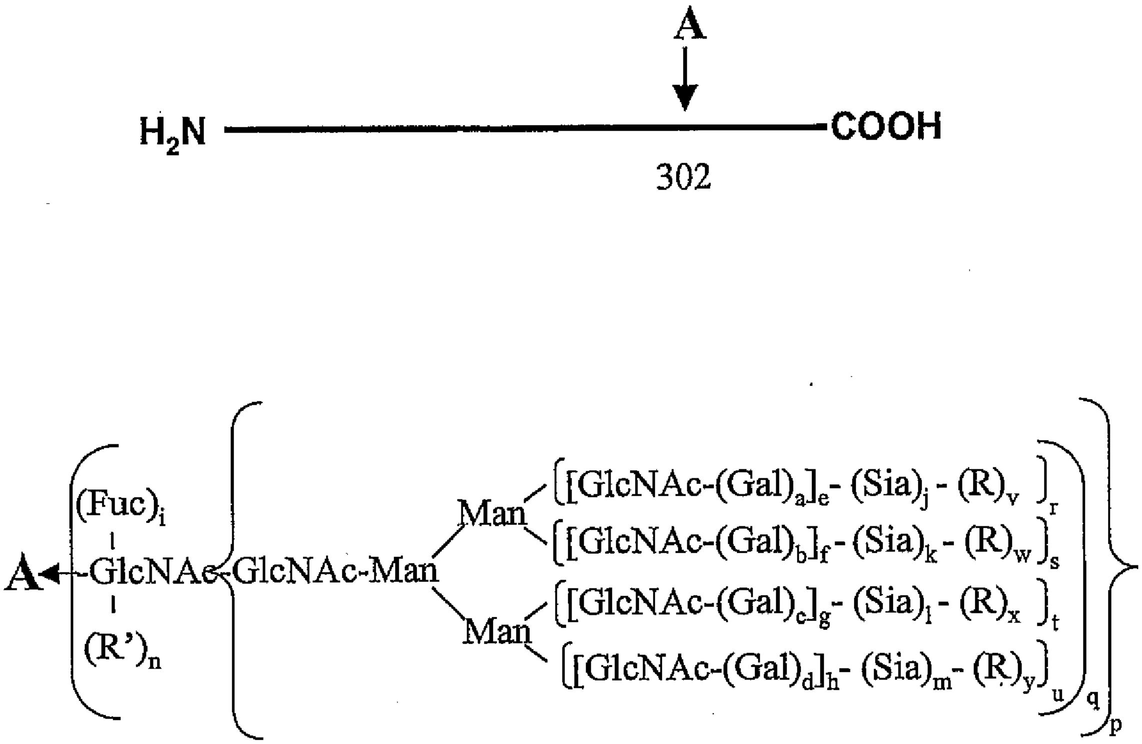


CHO, BHK, 293 cells, Vero expressed Urokinase.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. CMP-SA, α2,8-ST

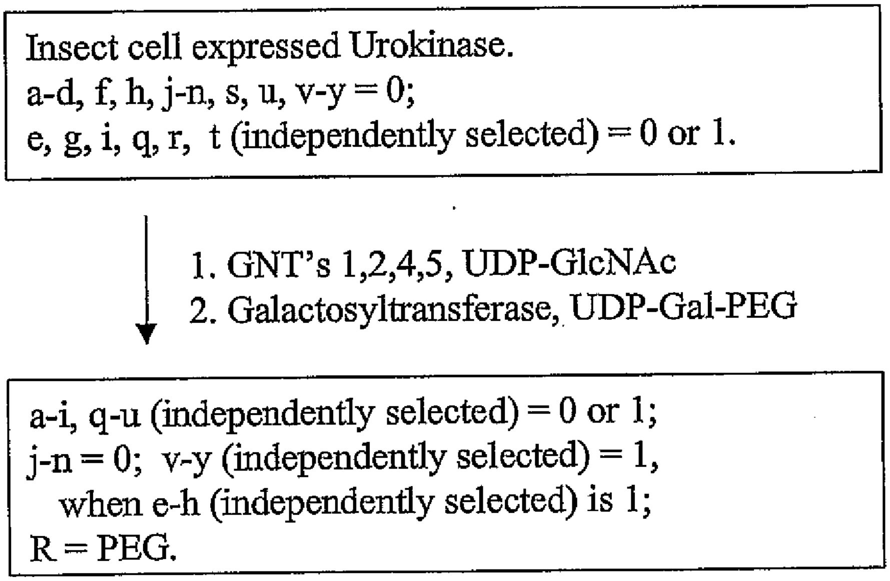
a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1;
j-m (independently selected) = 0-20;
v-y (independently selected) = 0.

FIG. 41G


A
H2N
COOH
302
A
(Fuc)i
GlcNAc
(R')n
GlcNAc-Man
Man
Man
[[GlcNAc-(Gal)a]e- (Sia)j - (R)v]r
[[GlcNAc-(Gal)b]f- (Sia)k - (R)w]s
[[GlcNAc-(Gal)c]g- (Sia)l - (R)x]t
[[GlcNAc-(Gal)d]h- (Sia)m- (R)y]u
q
p

a-d, i, n, p-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0;
R = modifying group, mannose, oligo-mannose;
R' = H, glycosyl residue, modifying group,
glycoconjugate.

FIG. 41H

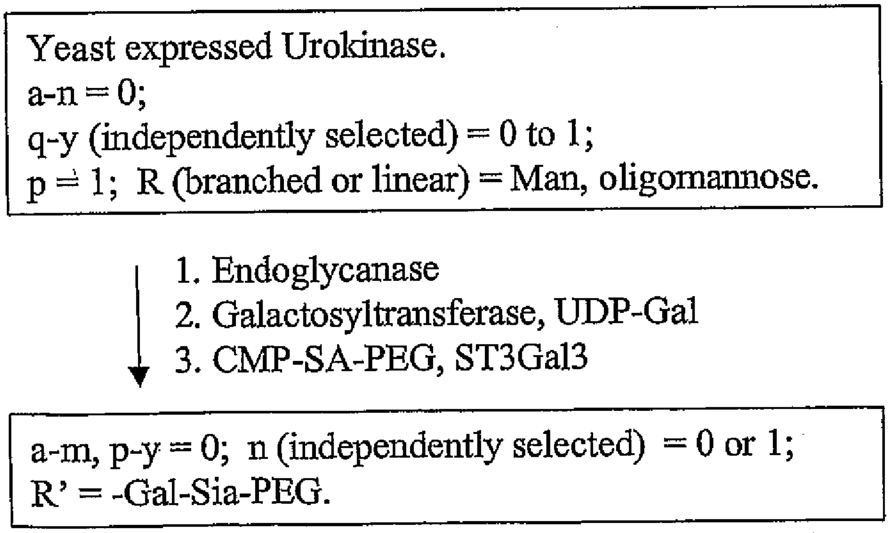


Insect cell expressed Urokinase.
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.

1. GNT's 1,2,4,5, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal-PEG

a-i, q-u (independently selected) = 0 or 1;
j-n = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.

FIG. 41I

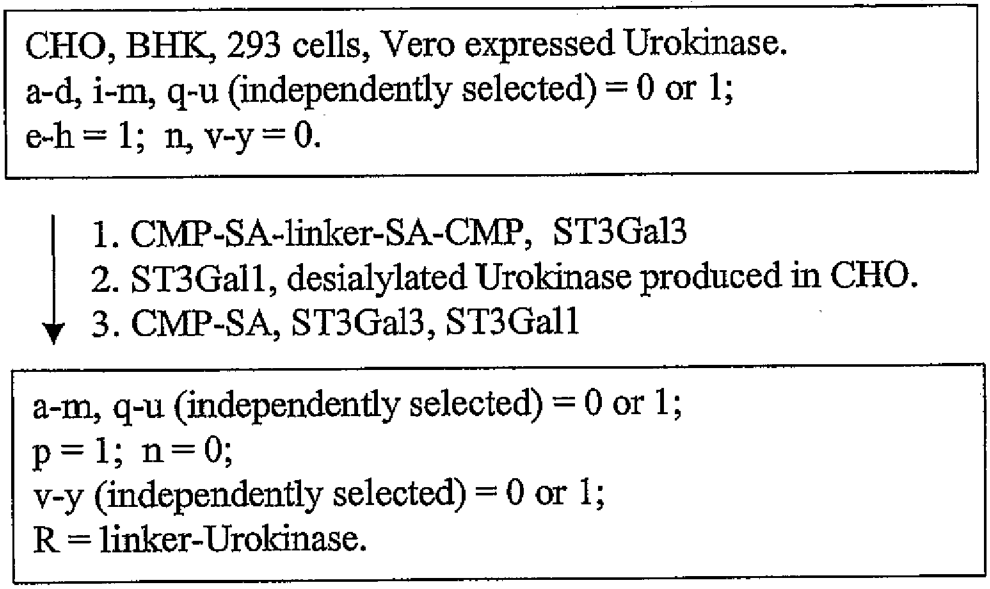


Yeast expressed Urokinase.
a-n = 0;
q-y (independently selected) = 0 to 1;
p = 1; R (branched or linear) = Man, oligomannose.

1. Endoglycanase
2. Galactosyltransferase, UDP-Gal
3. CMP-SA-PEG, ST3Gal3

a-m, p-y = 0; n (independently selected) = 0 or 1;
R' = -Gal-Sia-PEG.

FIG. 41J

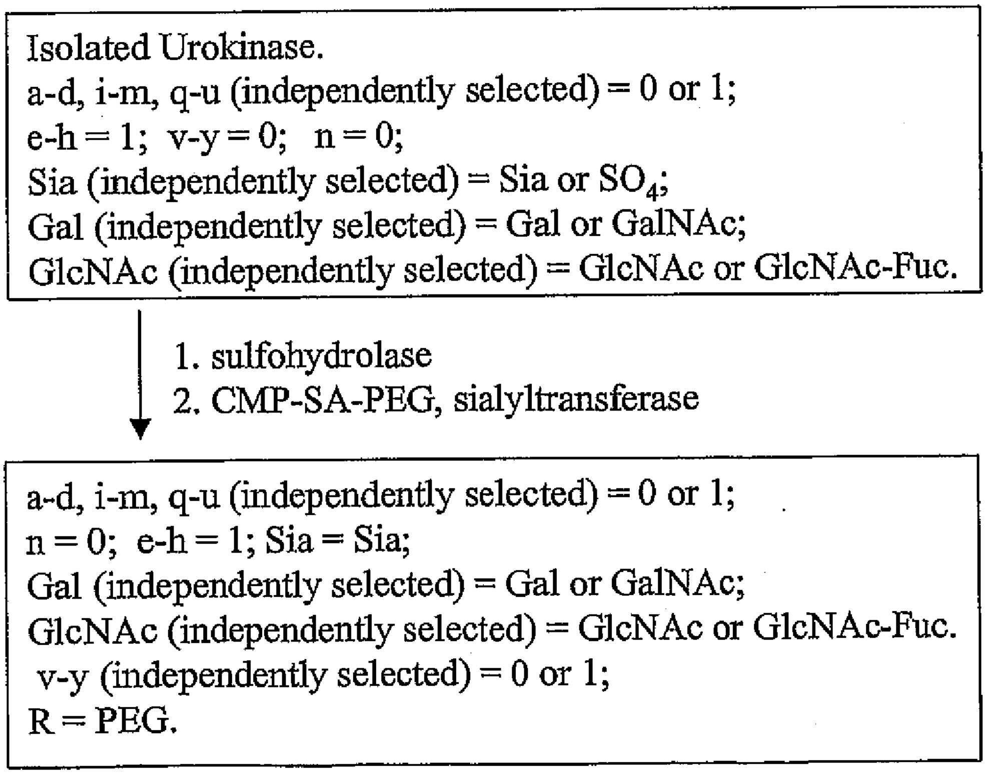


CHO, BHK, 293 cells, Vero expressed Urokinase.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; n, v-y = 0.

1. CMP-SA-linker-SA-CMP, ST3Gal3
2. ST3Gal1, desialylated Urokinase produced in CHO.
3. CMP-SA, ST3Gal3, ST3Gal1

a-m, q-u (independently selected) = 0 or 1;
p = 1; n = 0;
v-y (independently selected) = 0 or 1;
R = linker-Urokinase.

FIG. 41K

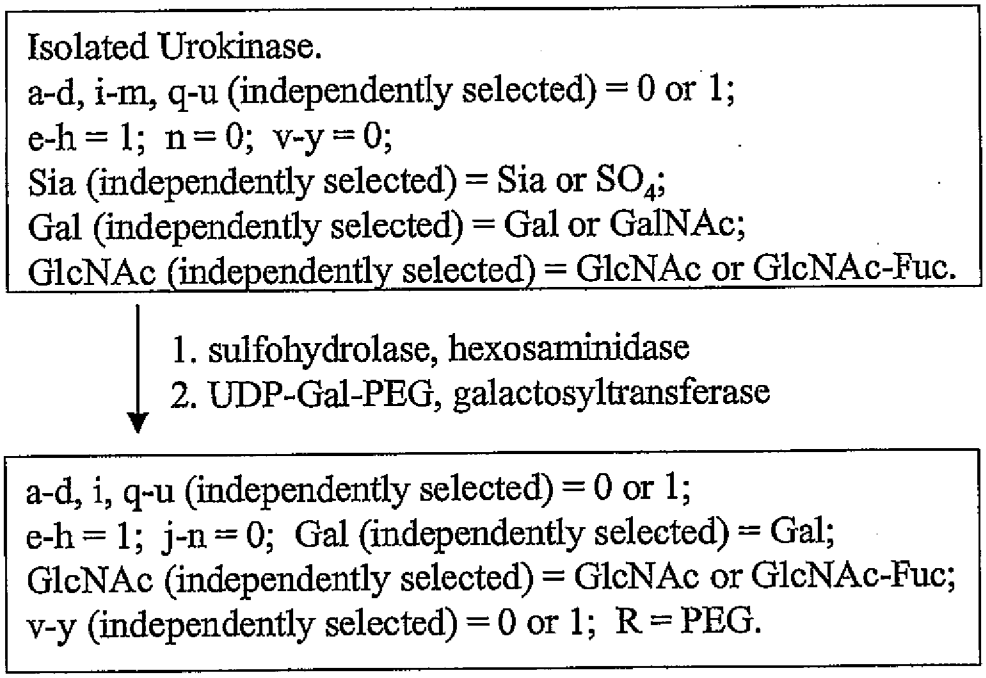


Isolated Urokinase.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0; n = 0;
Sia (independently selected) = Sia or SO_4;
Gal (independently selected) = Gal or GalNAc;
GlcNAc (independently selected) = GlcNAc or GlcNAc-Fuc.

1. sulfohydrolase
2. CMP-SA-PEG, sialyltransferase

a-d, i-m, q-u (independently selected) = 0 or 1;
n = 0; e-h = 1; Sia = Sia;
Gal (independently selected) = Gal or GalNAc;
GlcNAc (independently selected) = GlcNAc or GlcNAc-Fuc.
v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 41L

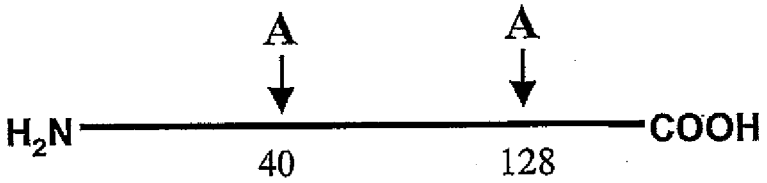


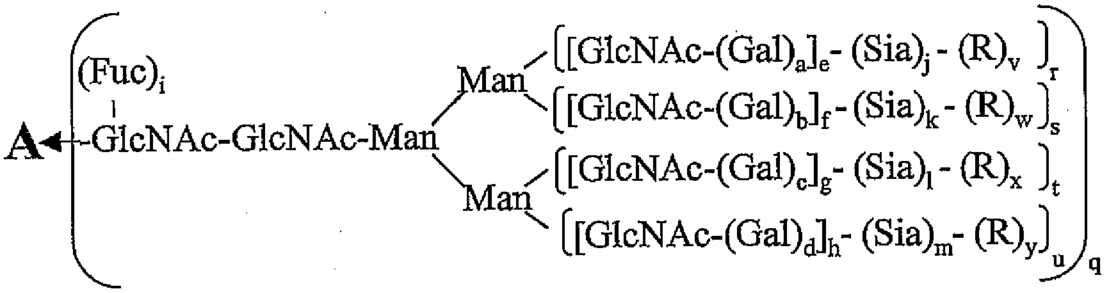
Isolated Urokinase.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; n = 0; v-y = 0;
Sia (independently selected) = Sia or SO_4;
Gal (independently selected) = Gal or GalNAc;
GlcNAc (independently selected) = GlcNAc or GlcNAc-Fuc.

1. sulfohydrolase, hexosaminidase
2. UDP-Gal-PEG, galactosyltransferase

a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1; j-n = 0; Gal (independently selected) = Gal;
GlcNAc (independently selected) = GlcNAc or GlcNAc-Fuc;
v-y (independently selected) = 0 or 1; R = PEG.

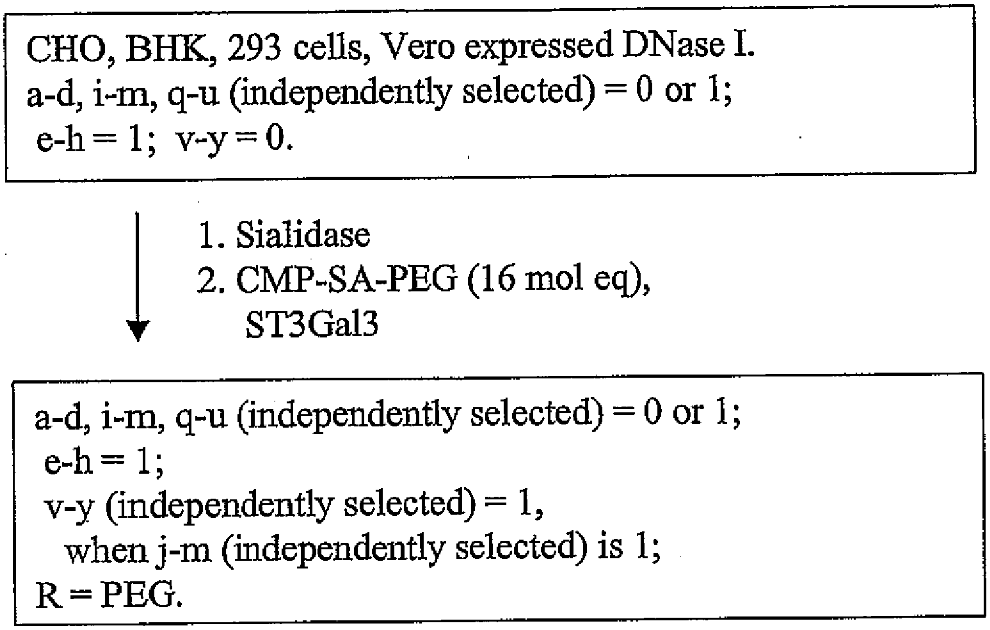
FIG. 41M




(Fuc)i
A
-GlcNAc-GlcNAc-Man
Man
Man
[[GlcNAc-(Gal)a]e- (Sia)j - (R)v]r
[[GlcNAc-(Gal)b]f - (Sia)k - (R)w]s
[[GlcNAc-(Gal)c]g- (Sia)l - (R)x]t
[[GlcNAc-(Gal)d]h- (Sia)m- (R)y]u
q

a-d, i, q-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0; R = polymer, glycoconjugate.

FIG. 42A

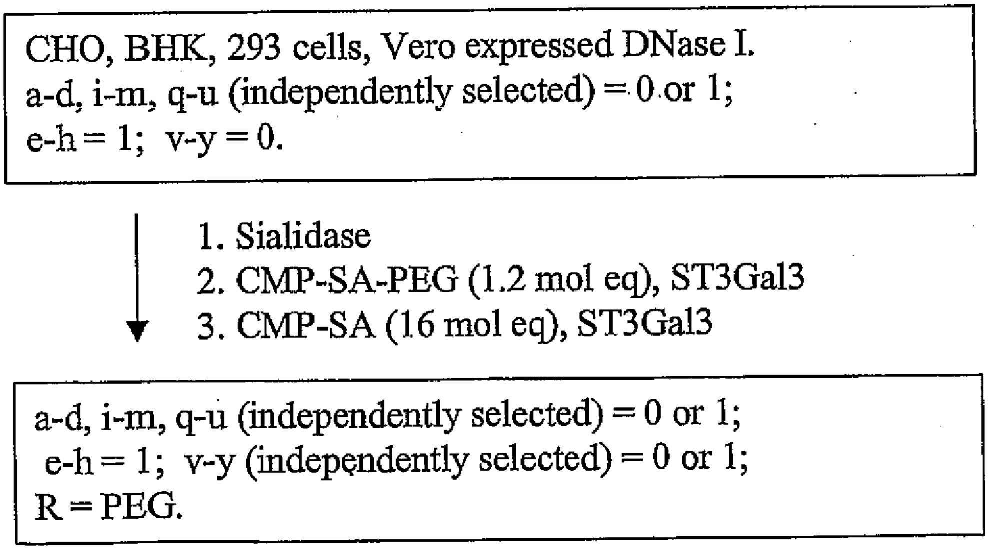


CHO, BHK, 293 cells, Vero expressed DNase I.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. Sialidase
2. CMP-SA-PEG (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1;
v-y (independently selected) = 1, when j-m (independently selected) is 1;
R = PEG.

FIG. 42B



CHO, BHK, 293 cells, Vero expressed DNase I.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. Sialidase
2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
3. CMP-SA (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 42C

NSO expressed DNase I.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0;
Sia (independently selected) = Sia or Gal.

1. Sialidase and α-galactosidase
2. α-Galactosyltransferase, UDP-Gal
3. CMP-SA-PEG, ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.

FIG. 42D

CHO, BHK, 293 cells, Vero expressed DNase I.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. Sialidase
2. CMP-SA-PEG (16 mol eq), ST3Gal3
3. CMP-SA, ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 42E

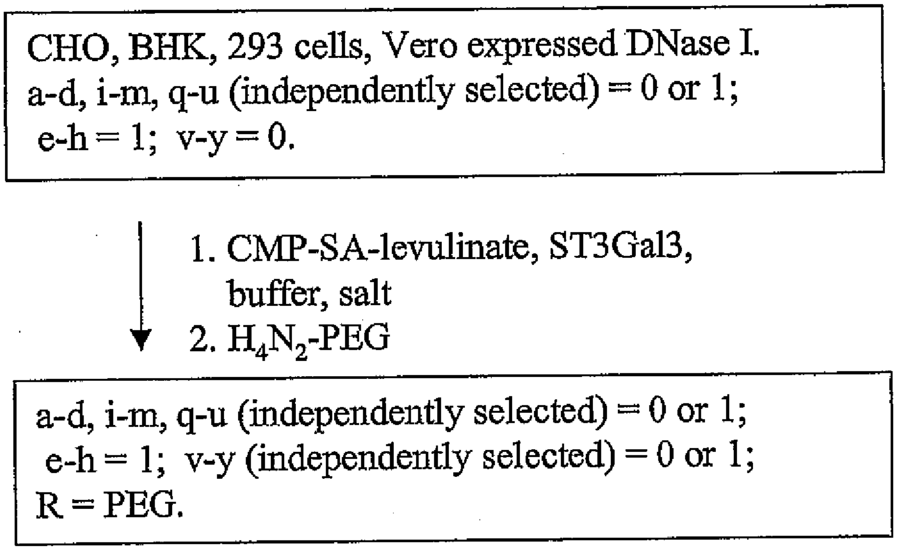

CHO, BHK, 293 cells, Vero expressed DNase I.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
1. CMP-SA-levulinate, ST3Gal3, buffer, salt
2. H_4N_2-PEG
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.

FIG. 42F

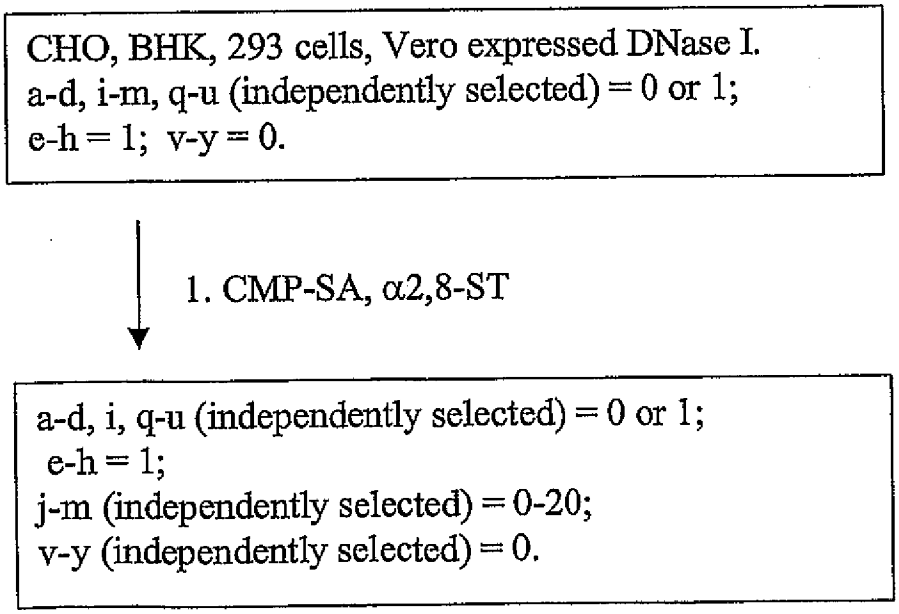
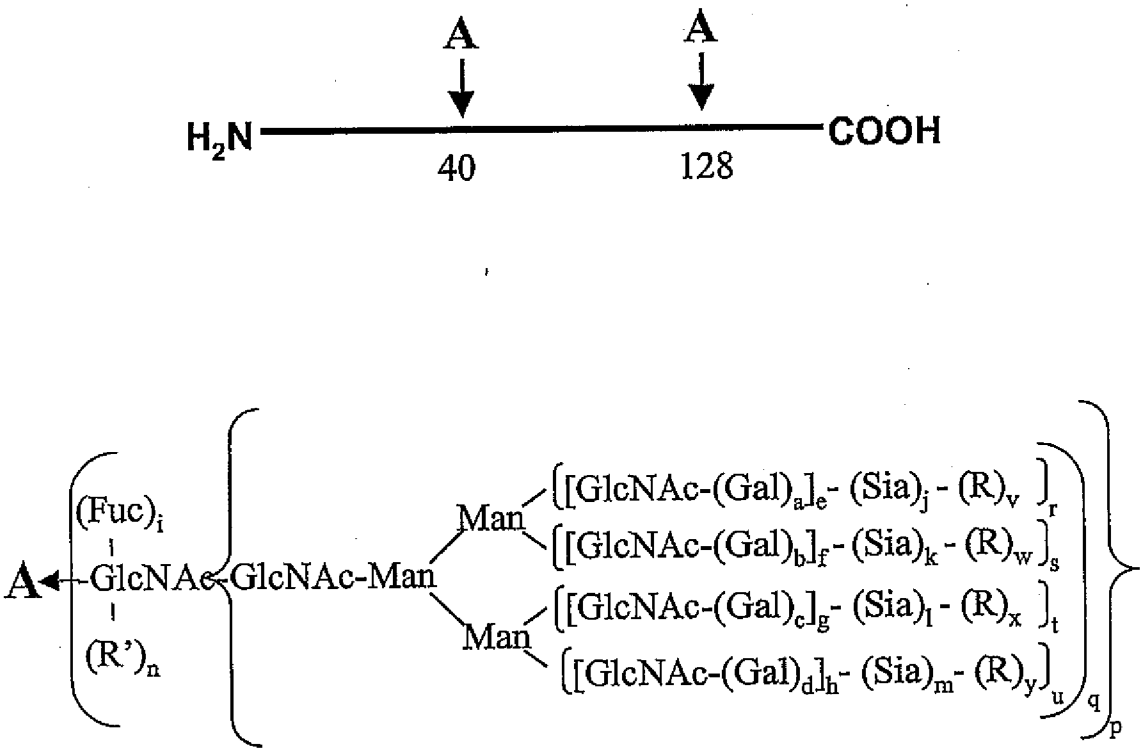

CHO, BHK, 293 cells, Vero expressed DNase I.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
1. CMP-SA, α2,8-ST
a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1;
j-m (independently selected) = 0-20;
v-y (independently selected) = 0.

FIG. 42G


A
A
H2N
COOH
40
128
A
(Fuc)i
GlcNAc
(R')n
GlcNAc-Man
Man
Man
[[GlcNAc-(Gal)a]e- (Sia)j - (R)v]r
[[GlcNAc-(Gal)b]f- (Sia)k - (R)w]s
[[GlcNAc-(Gal)c]g- (Sia)l - (R)x]t
[[GlcNAc-(Gal)d]h- (Sia)m- (R)y]u
q
p

a-d, i, n, p-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0;
R = modifying group, mannose, oligo-mannose;
R' = H, glycosyl residue, modifying group,
glycoconjugate.

FIG. 42H

Insect cell expressed DNase I.
a-d, f, h, j-n, s, u, v-y' = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.

↓
1. GNT's 1,2,4,5, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal-PEG

a-i, q-u (independently selected) = 0 or 1; j-n = 0;
v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.

FIG. 42I

Yeast expressed DNase I.
a-n = 0;
q-y (independently selected) = 0 to 1;
p = 1; R (branched or linear) = Man, oligomannose.

↓
1. Endoglycanase
2. Galactosyltransferase, UDP-Gal
3. CMP-SA-PEG, ST3Gal3

a-n, p-y = 0; n (independently selected) = 0 or 1;
R' = -Gal-Sia-PEG.

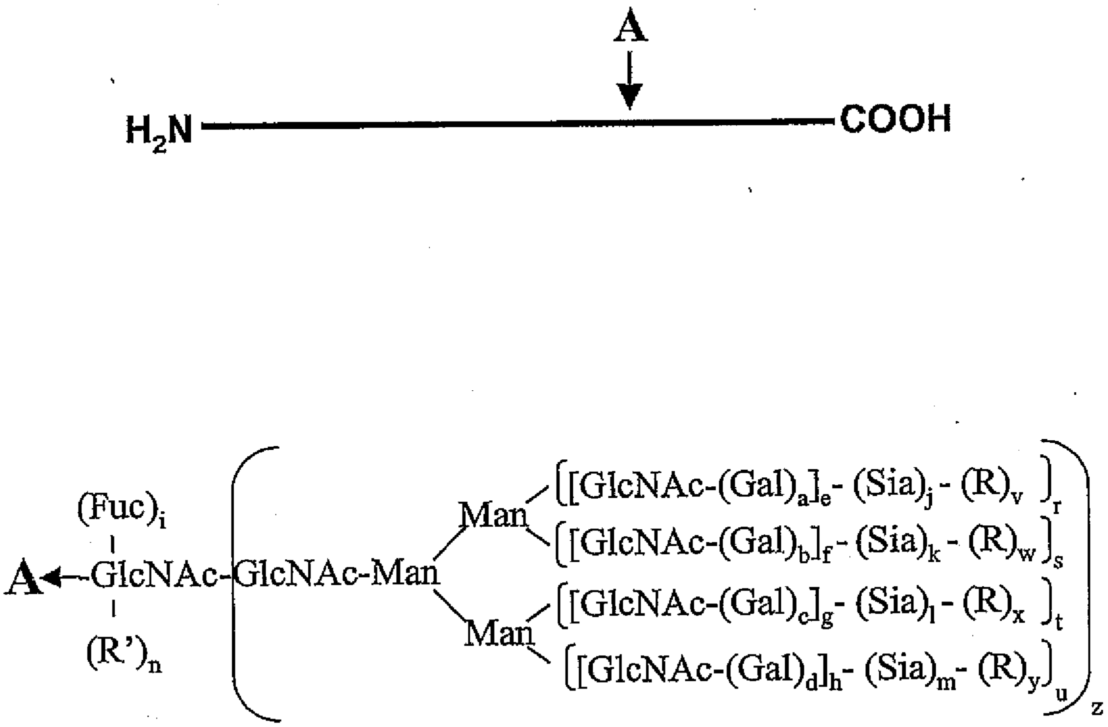
FIG. 42J

CHO, BHK, 293 cells, Vero expressed DNase I.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; n, v-y = 0.

1. CMP-SA-linker-SA-CMP, ST3Gal3
2. ST3Gal1, desialylated alpha-1-Proteinase inhibitor.
3. CMP-SA, ST3Gal3, ST3Gal1

a-m, q-u (independently selected) = 0 or 1;
p = 1; n = 0;
v-y (independently selected) = 0 or 1;
R = linker- alpha-1-Proteinase inhibitor.

FIG. 42K


A
H2N
COOH
(Fuc)i
A
GlcNAc-GlcNAc-Man
(R')n
Man
Man
[[GlcNAc-(Gal)a]e- (Sia)j - (R)v]r
[[GlcNAc-(Gal)b]f - (Sia)k - (R)w]s
[[GlcNAc-(Gal)c]g- (Sia)l - (R)x]t
[[GlcNAc-(Gal)d]h- (Sia)m- (R)y]u
z

a-d, i, r-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
j-m (independently selected) = 0 or 1.
n, v-y = 0; z = 0 or 1;
R = modifying group, mannose, oligo-mannose;
R' = H, glycosyl residue, modifying group,
glycoconjugate.

FIG. 43A

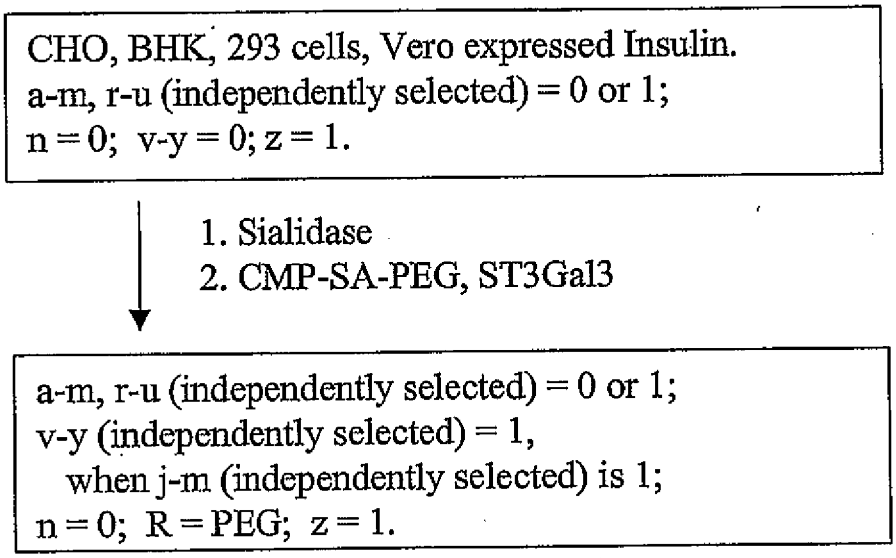

CHO, BHK, 293 cells, Vero expressed Insulin.
a-m, r-u (independently selected) = 0 or 1;
n = 0; v-y = 0; z = 1.
1. Sialidase
2. CMP-SA-PEG, ST3Gal3
a-m, r-u (independently selected) = 0 or 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
n = 0; R = PEG; z = 1.

FIG. 43B

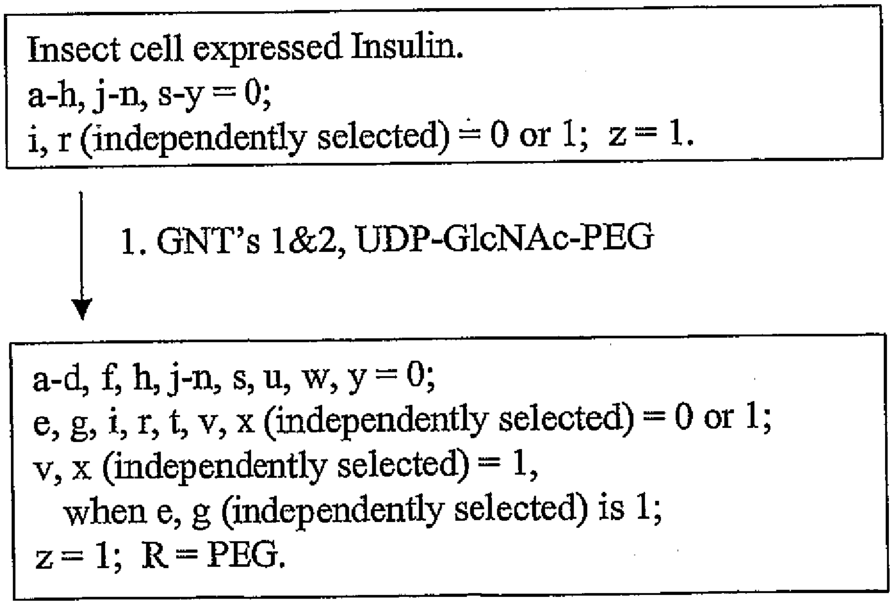
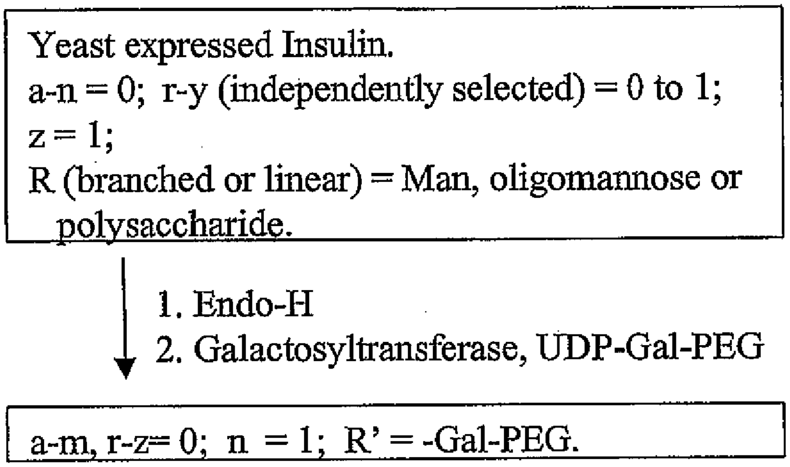

Insect cell expressed Insulin.
a-h, j-n, s-y = 0;
i, r (independently selected) = 0 or 1; z = 1.
1. GNT's 1&2, UDP-GlcNAc-PEG
a-d, f, h, j-n, s, u, w, y = 0;
e, g, i, r, t, v, x (independently selected) = 0 or 1;
v, x (independently selected) = 1,
when e, g (independently selected) is 1;
z = 1; R = PEG.

FIG. 43C

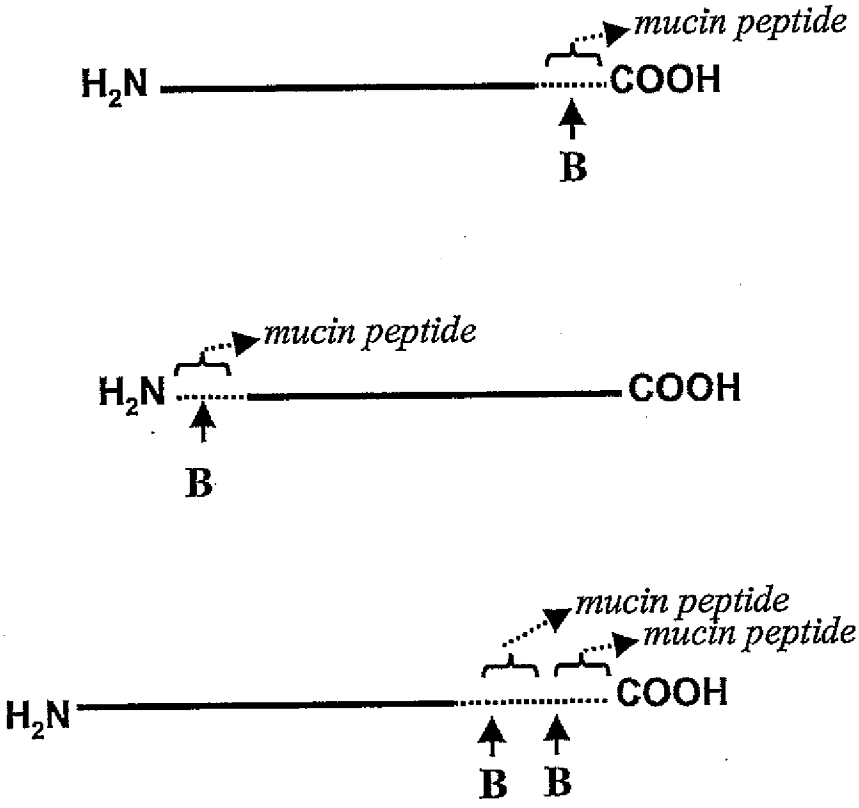


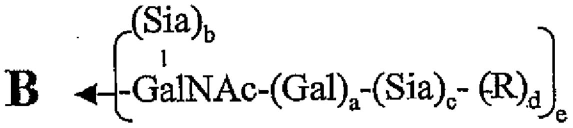
Yeast expressed Insulin.
a-n = 0; r-y (independently selected) = 0 to 1;
z = 1;
R (branched or linear) = Man, oligomannose or polysaccharide.

1. Endo-H
2. Galactosyltransferase, UDP-Gal-PEG

a-m, r-z= 0; n = 1; R' = -Gal-PEG.

FIG. 43D

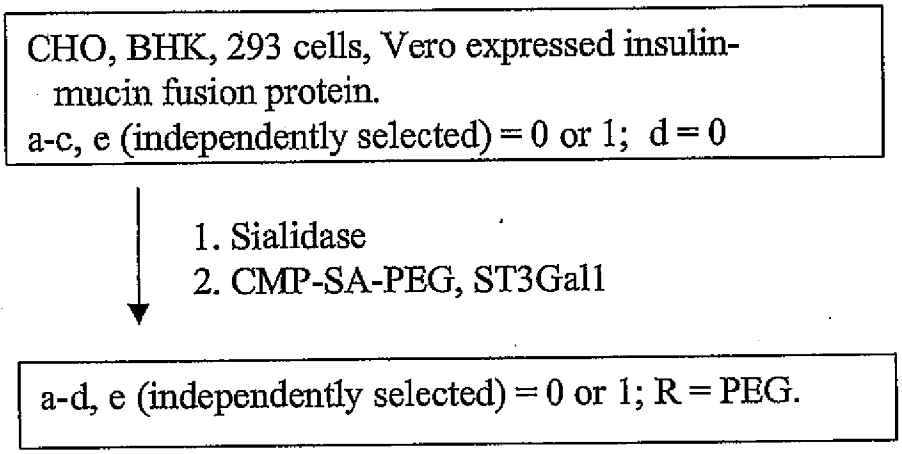




$$\mathbf{B} \leftarrow \left[-\overset{(\mathrm{Sia})_b}{\mathrm{GalNAc}}-(\mathrm{Gal})_a-(\mathrm{Sia})_c-(\mathrm{R})_d \right]_e$$

a-c, e (independently selected) = 0 or 1;
d = 0; R = polymer

FIG. 43E

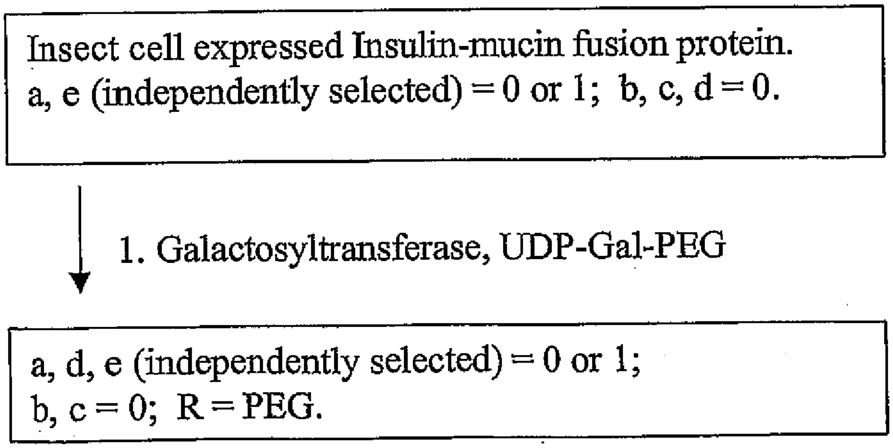


CHO, BHK, 293 cells, Vero expressed insulin-mucin fusion protein.
a-c, e (independently selected) = 0 or 1; d = 0

1. Sialidase
2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 43F



Insect cell expressed Insulin-mucin fusion protein.
a, e (independently selected) = 0 or 1; b, c, d = 0.

1. Galactosyltransferase, UDP-Gal-PEG

a, d, e (independently selected) = 0 or 1;
b, c = 0; R = PEG.

FIG. 43G

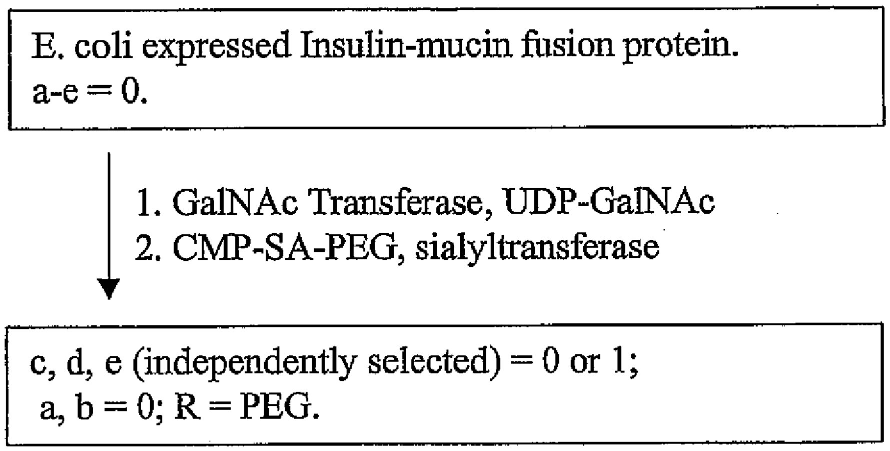
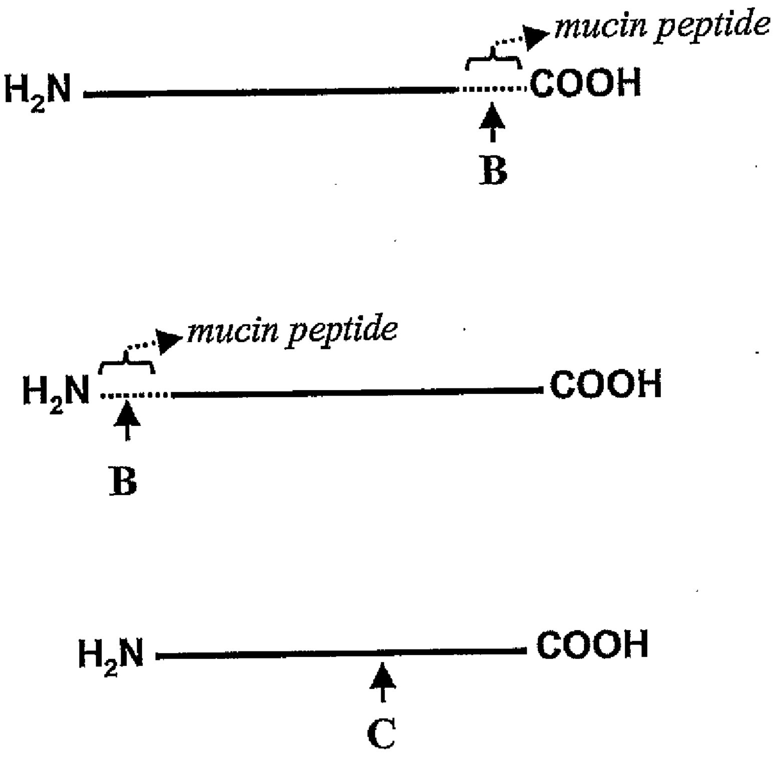
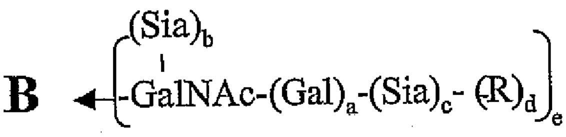

E. coli expressed Insulin-mucin fusion protein.
a-e = 0.
1. GalNAc Transferase, UDP-GalNAc
2. CMP-SA-PEG, sialyltransferase
c, d, e (independently selected) = 0 or 1;
a, b = 0; R = PEG.

FIG. 43H





$$\mathbf{B} \leftarrow \left[-\overset{(\mathrm{Sia})_b}{\mathrm{GalNAc}}-(\mathrm{Gal})_a-(\mathrm{Sia})_c-(\mathrm{R})_d \right]_e$$

$\mathbf{C} \leftarrow (\mathrm{R'})_n$

a-c, e (independently selected) = 0 or 1;
d = 0; R = modifying group, mannose,
oligo-mannose.

FIG. 43I

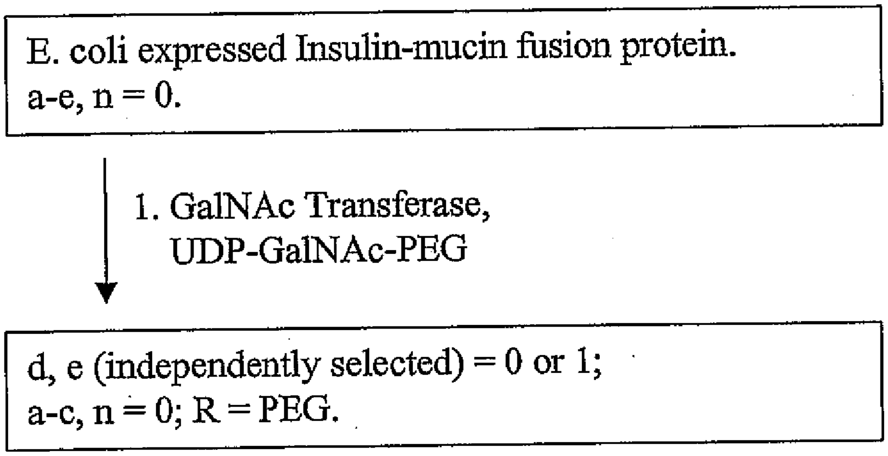

E. coli expressed Insulin-mucin fusion protein.
a-e, n = 0.
1. GalNAc Transferase,
UDP-GalNAc-PEG
d, e (independently selected) = 0 or 1;
a-c, n = 0; R = PEG.

FIG. 43J

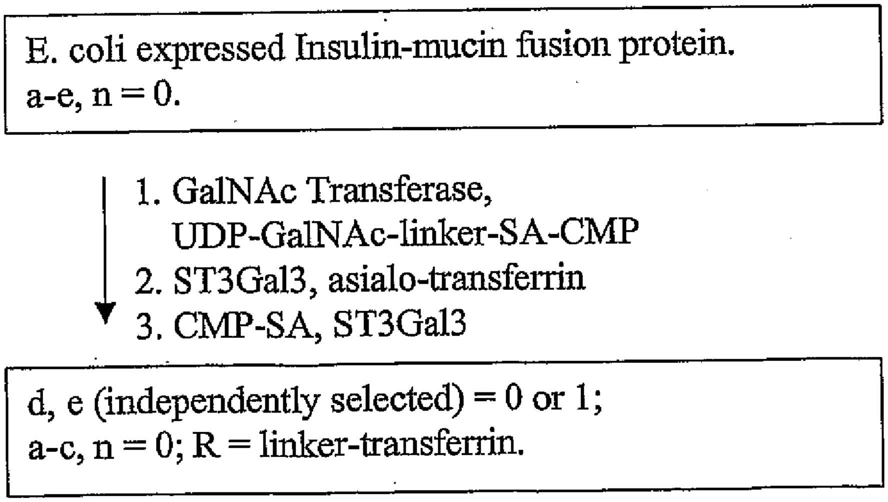

E. coli expressed Insulin-mucin fusion protein.
a-e, n = 0.
1. GalNAc Transferase,
UDP-GalNAc-linker-SA-CMP
2. ST3Gal3, asialo-transferrin
3. CMP-SA, ST3Gal3
d, e (independently selected) = 0 or 1;
a-c, n = 0; R = linker-transferrin.

FIG. 43K

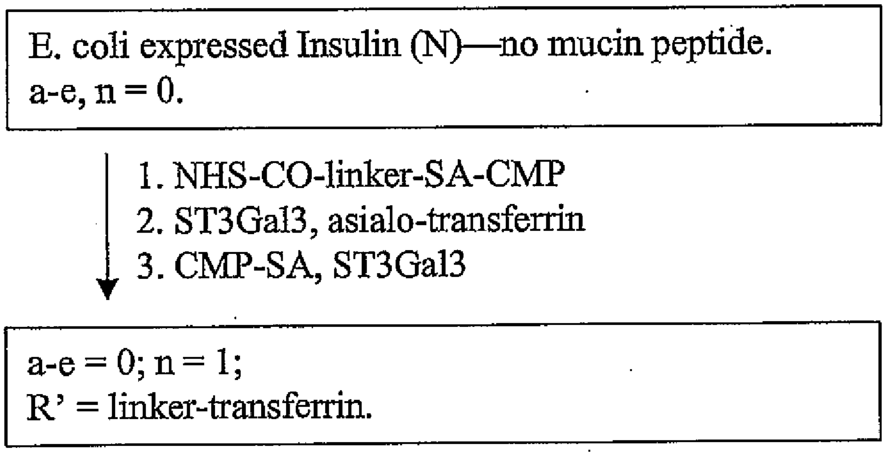
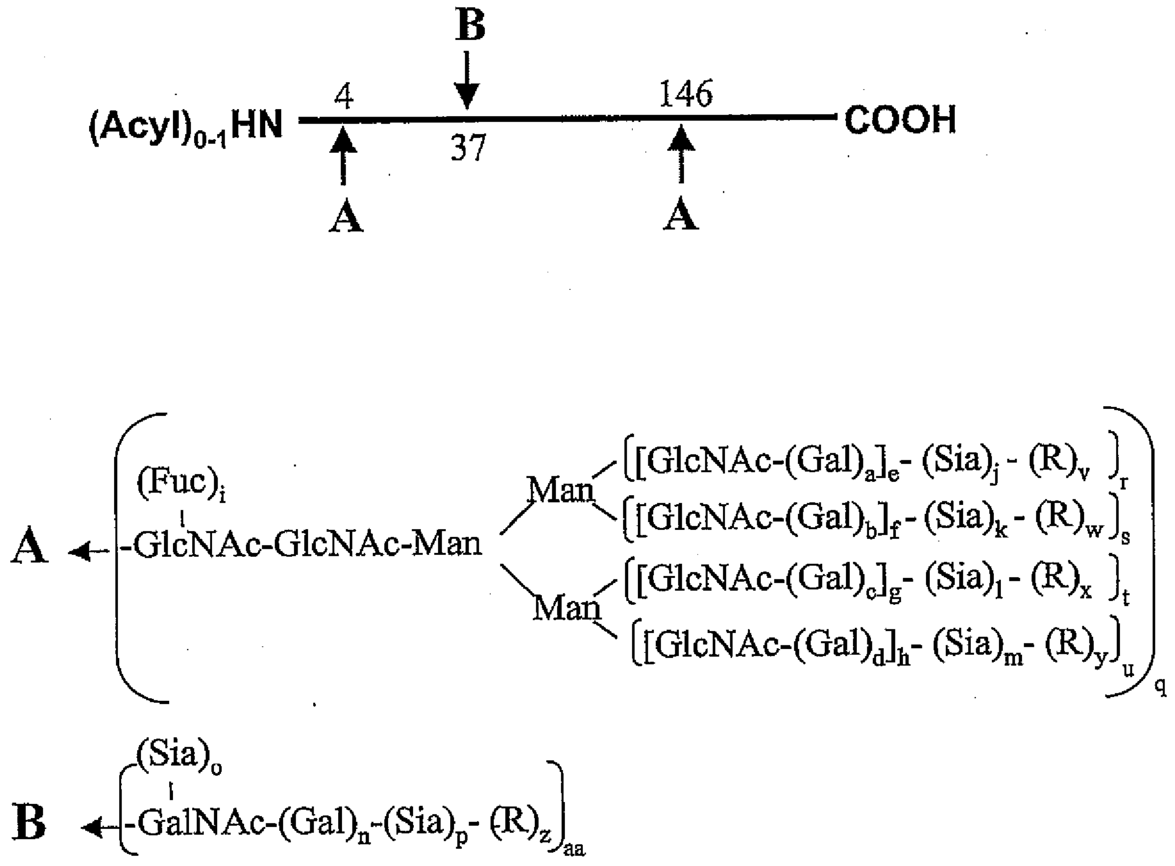
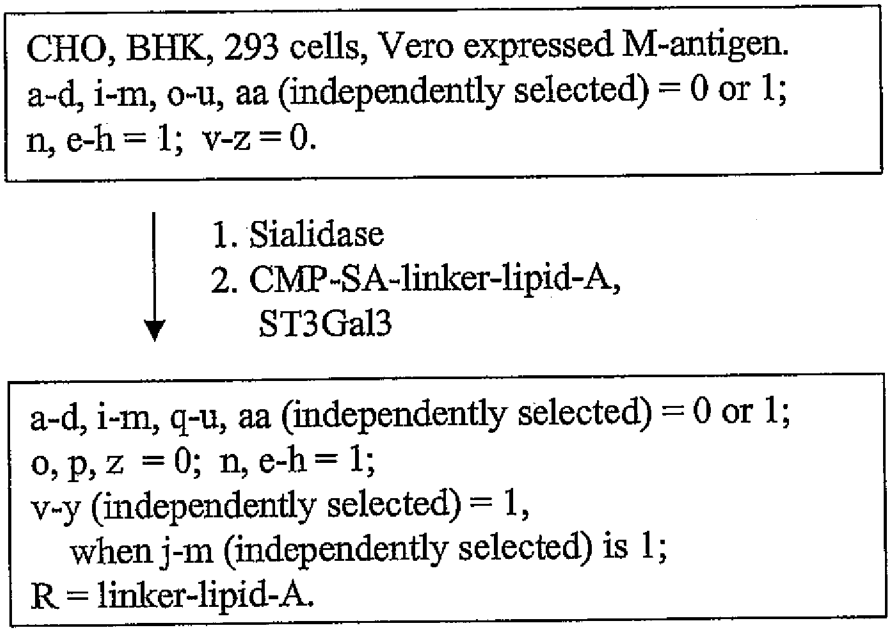

E. coli expressed Insulin (N)—no mucin peptide.
a-e, n = 0.
1. NHS-CO-linker-SA-CMP
2. ST3Gal3, asialo-transferrin
3. CMP-SA, ST3Gal3
a-e = 0; n = 1;
R' = linker-transferrin.

FIG. 43L


B
(Acyl)0-1HN
4
37
146
COOH
A
A
A
(Fuc)i
-GlcNAc-GlcNAc-Man
Man
[[GlcNAc-(Gal)a]e- (Sia)j - (R)v]r
[[GlcNAc-(Gal)b]f - (Sia)k - (R)w]s
Man
[[GlcNAc-(Gal)c]g- (Sia)l - (R)x]t
[[GlcNAc-(Gal)d]h- (Sia)m- (R)y]u
q
B
(Sia)o
-GalNAc-(Gal)n-(Sia)p- (R)z
aa

a-d, i, n-u, aa (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0; R = polymer, glycoconjugate.

FIG. 44A

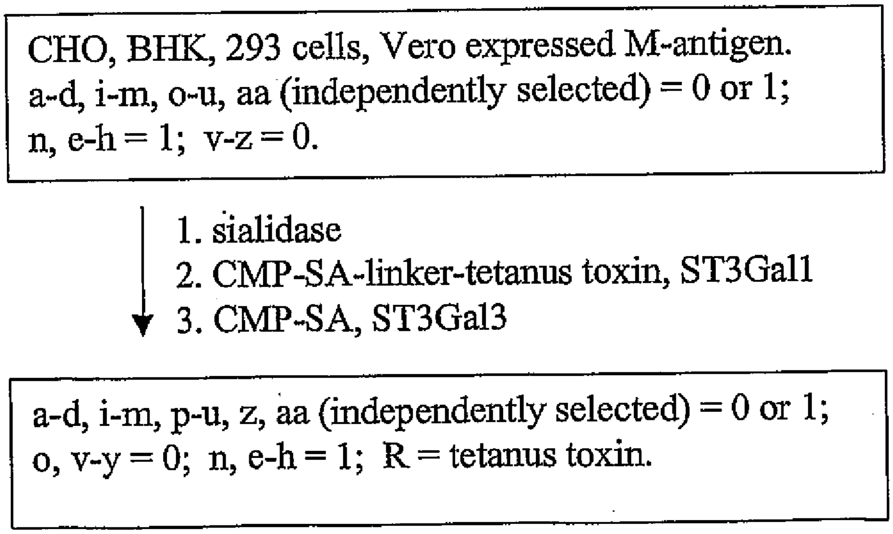


CHO, BHK, 293 cells, Vero expressed M-antigen.
a-d, i-m, o-u, aa (independently selected) = 0 or 1;
n, e-h = 1; v-z = 0.

1. Sialidase
2. CMP-SA-linker-lipid-A, ST3Gal3

a-d, i-m, q-u, aa (independently selected) = 0 or 1;
o, p, z = 0; n, e-h = 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = linker-lipid-A.

FIG. 44B

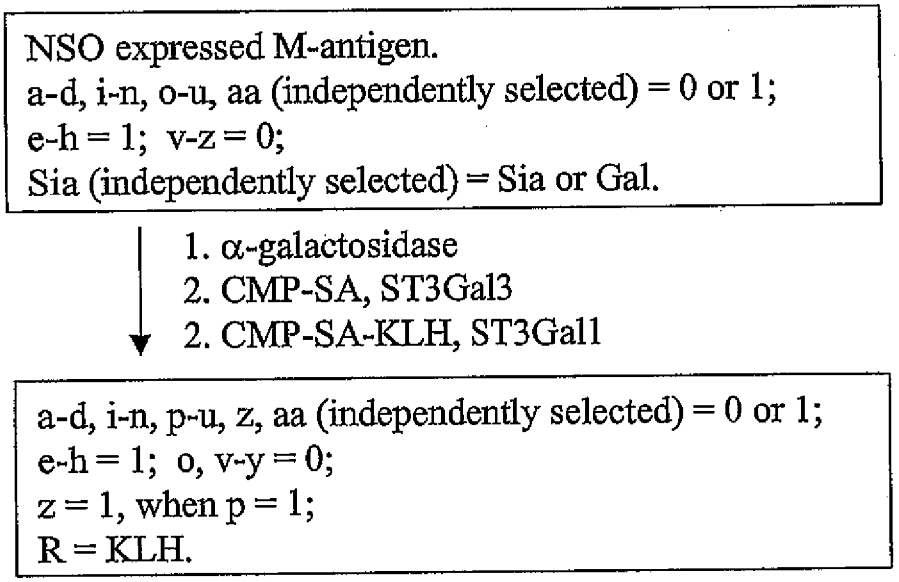


CHO, BHK, 293 cells, Vero expressed M-antigen.
a-d, i-m, o-u, aa (independently selected) = 0 or 1;
n, e-h = 1; v-z = 0.

1. sialidase
2. CMP-SA-linker-tetanus toxin, ST3Gal1
3. CMP-SA, ST3Gal3

a-d, i-m, p-u, z, aa (independently selected) = 0 or 1;
o, v-y = 0; n, e-h = 1; R = tetanus toxin.

FIG. 44C

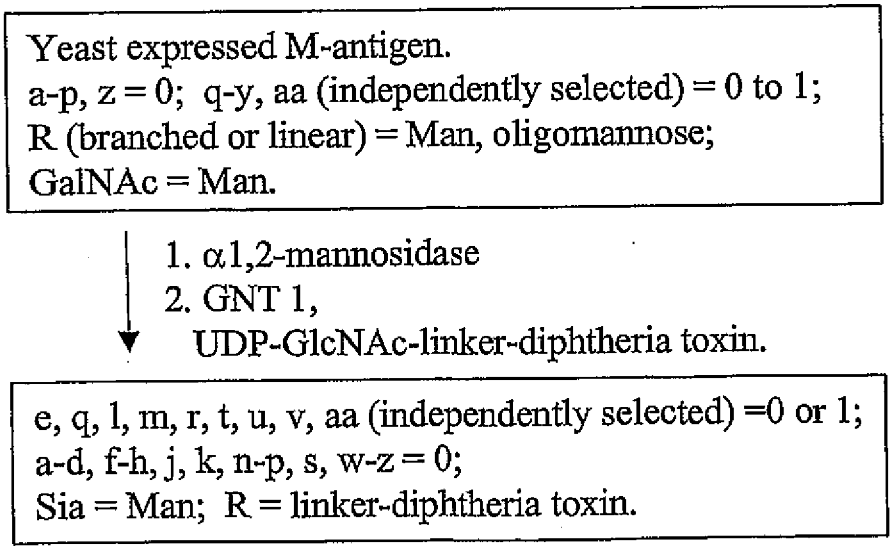


NSO expressed M-antigen.
a-d, i-n, o-u, aa (independently selected) = 0 or 1;
e-h = 1; v-z = 0;
Sia (independently selected) = Sia or Gal.

1. α-galactosidase
2. CMP-SA, ST3Gal3
2. CMP-SA-KLH, ST3Gal1

a-d, i-n, p-u, z, aa (independently selected) = 0 or 1;
e-h = 1; o, v-y = 0;
z = 1, when p = 1;
R = KLH.

FIG. 44D

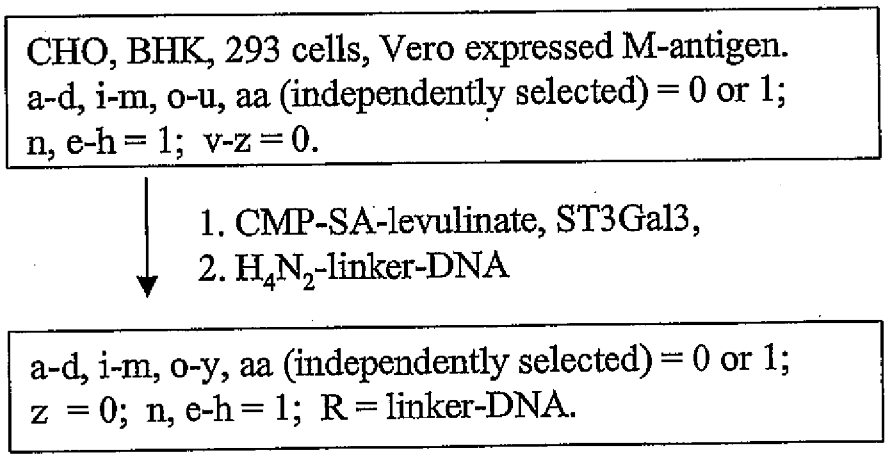


Yeast expressed M-antigen.
a-p, z = 0; q-y, aa (independently selected) = 0 to 1;
R (branched or linear) = Man, oligomannose;
GalNAc = Man.

1. α1,2-mannosidase
2. GNT 1,
UDP-GlcNAc-linker-diphtheria toxin.

e, q, l, m, r, t, u, v, aa (independently selected) =0 or 1;
a-d, f-h, j, k, n-p, s, w-z = 0;
Sia = Man; R = linker-diphtheria toxin.

FIG. 44E

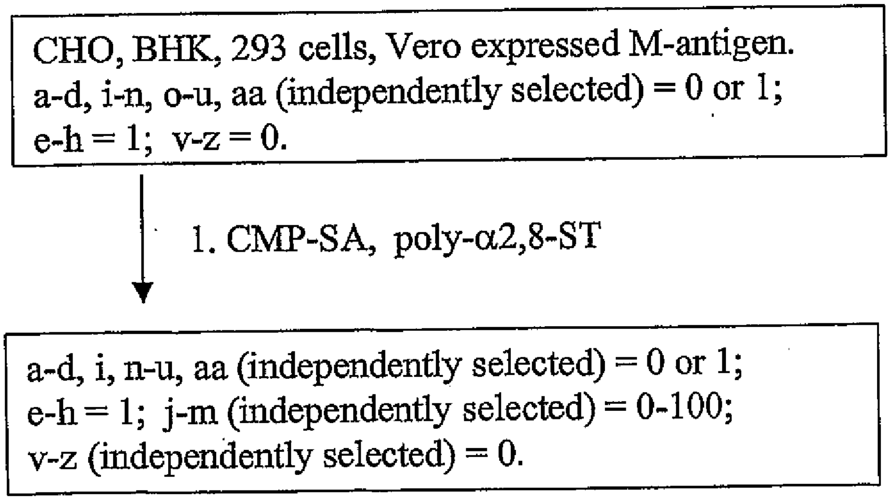


CHO, BHK, 293 cells, Vero expressed M-antigen.
a-d, i-m, o-u, aa (independently selected) = 0 or 1;
n, e-h = 1; v-z = 0.

1. CMP-SA-levulinate, ST3Gal3,
2. H_4N_2-linker-DNA

a-d, i-m, o-y, aa (independently selected) = 0 or 1;
z = 0; n, e-h = 1; R = linker-DNA.

FIG. 44F

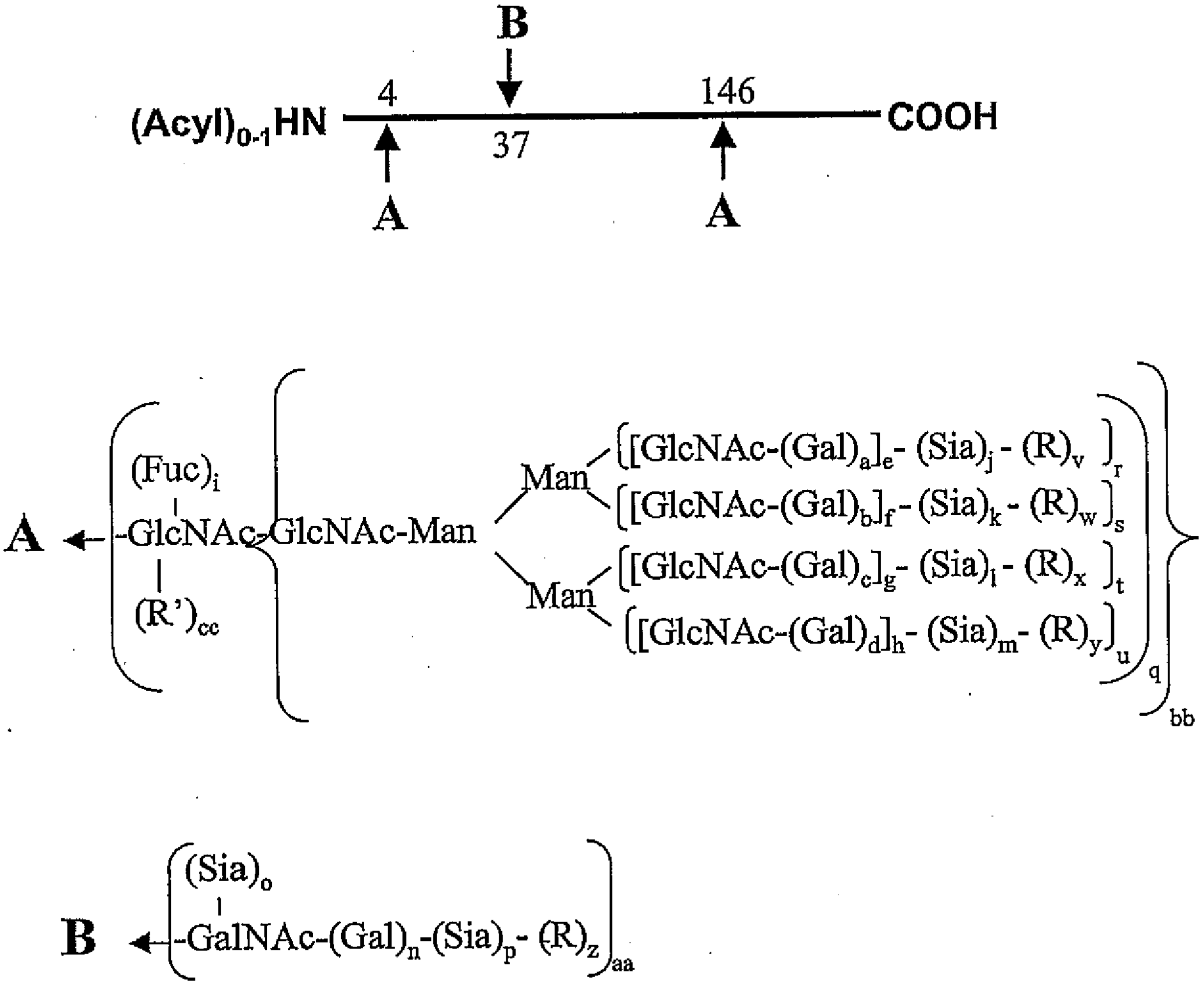


CHO, BHK, 293 cells, Vero expressed M-antigen.
a-d, i-n, o-u, aa (independently selected) = 0 or 1;
e-h = 1; v-z = 0.

1. CMP-SA, poly-α2,8-ST

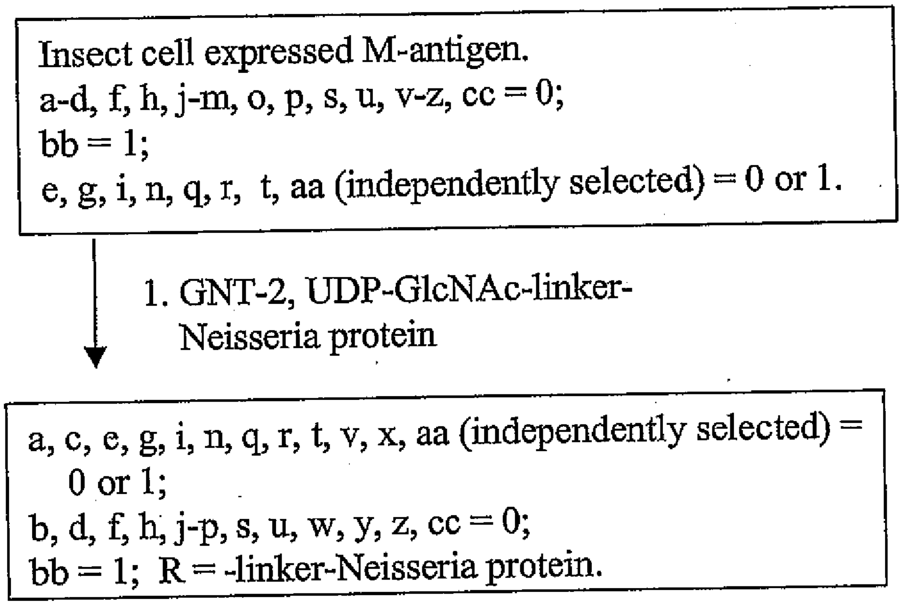
a-d, i, n-u, aa (independently selected) = 0 or 1;
e-h = 1; j-m (independently selected) = 0-100;
v-z (independently selected) = 0.

FIG. 44G


B
(Acyl)0-1HN
4
37
146
COOH
A
A
(Fuc)i
A ← -GlcNAc-GlcNAc-Man
(R')cc
Man
[[GlcNAc-(Gal)a]e- (Sia)j - (R)v]r
[[GlcNAc-(Gal)b]f- (Sia)k - (R)w]s
Man
[[GlcNAc-(Gal)c]g- (Sia)l - (R)x]t
[[GlcNAc-(Gal)d]h- (Sia)m- (R)y]u
q
bb
(Sia)o
B ← -GalNAc-(Gal)n-(Sia)p- (R)z
aa

a-d, i, n, q-u, aa, bb, (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-p (independently selected) = 0 to 100.
Cc, v-y = 0;
R = modifying group, mannose, oligo-mannose.
R'= H, glycosyl residue, modifying group, glycoconjugate.

FIG. 44H

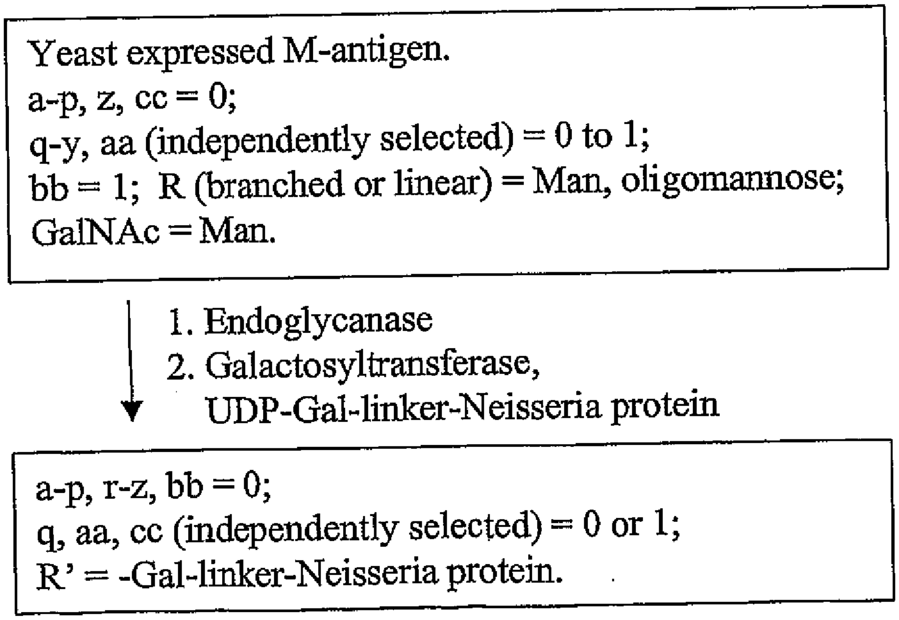


Insect cell expressed M-antigen.
a-d, f, h, j-m, o, p, s, u, v-z, cc = 0;
bb = 1;
e, g, i, n, q, r, t, aa (independently selected) = 0 or 1.

1. GNT-2, UDP-GlcNAc-linker-Neisseria protein

a, c, e, g, i, n, q, r, t, v, x, aa (independently selected) = 0 or 1;
b, d, f, h, j-p, s, u, w, y, z, cc = 0;
bb = 1; R = -linker-Neisseria protein.

FIG. 44I



Yeast expressed M-antigen.
a-p, z, cc = 0;
q-y, aa (independently selected) = 0 to 1;
bb = 1; R (branched or linear) = Man, oligomannose;
GalNAc = Man.

1. Endoglycanase
2. Galactosyltransferase, UDP-Gal-linker-Neisseria protein

a-p, r-z, bb = 0;
q, aa, cc (independently selected) = 0 or 1;
R' = -Gal-linker-Neisseria protein.

FIG. 44J

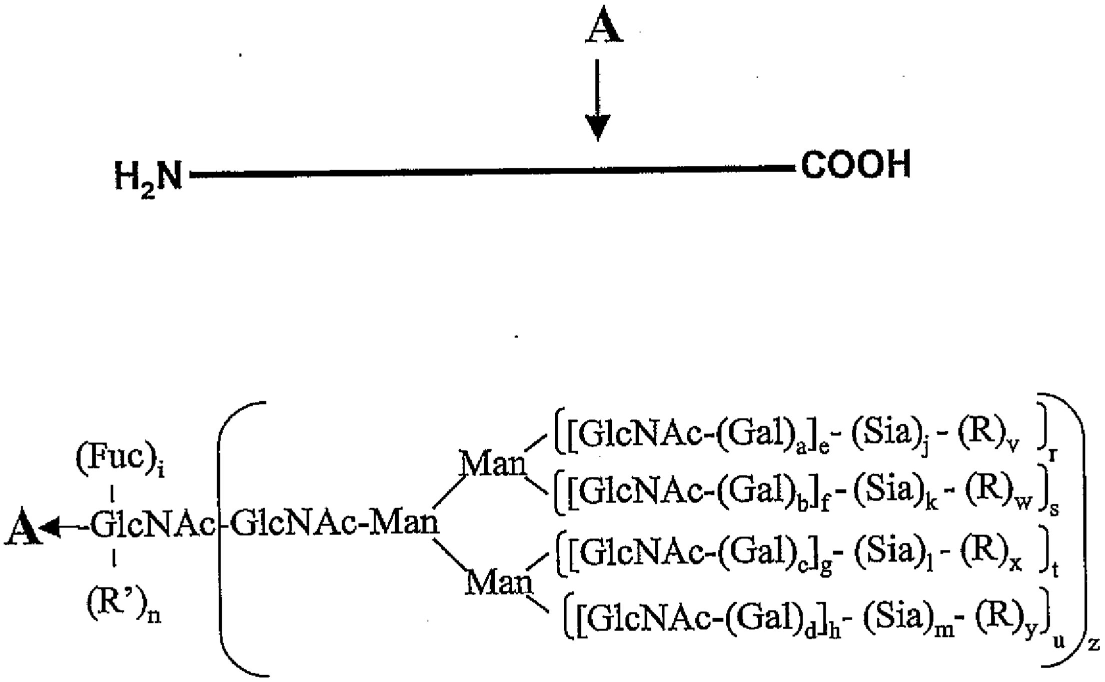
Yeast expressed M-antigen.
a-p, z, cc = 0;
q-y, aa (independently selected) = 0 to 1; bb = 1;
R (branched or linear) = Man, oligomannose;
GalNAc = Man.

↓

1. mannosidases
2. GNT 1 & 2, UDP-GlcNAc
3. UDP-Gal, Galactosyltransferase,
4. CMP-SA, sialyltransferase

a, c, e, g, j, l, q, r, t, aa (independently selected) = 0 or 1;
b, d, f, h, k, m-p, s, u-z, cc = 0; bb = 1.

FIG. 44K


A
H2N
COOH
(Fuc)i
A
GlcNAc
(R')n
GlcNAc-Man
Man
Man
[[GlcNAc-(Gal)a]e- (Sia)j - (R)v]r
[[GlcNAc-(Gal)b]f- (Sia)k - (R)w]s
[[GlcNAc-(Gal)c]g- (Sia)l - (R)x]t
[[GlcNAc-(Gal)d]h- (Sia)m- (R)y]u
z

a-d, i, r-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
j-m (independently selected) = 0 or 1.
n, v-y = 0; z = 0 or 1;
R = modifying group, mannose, oligo-mannose;
R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 45A

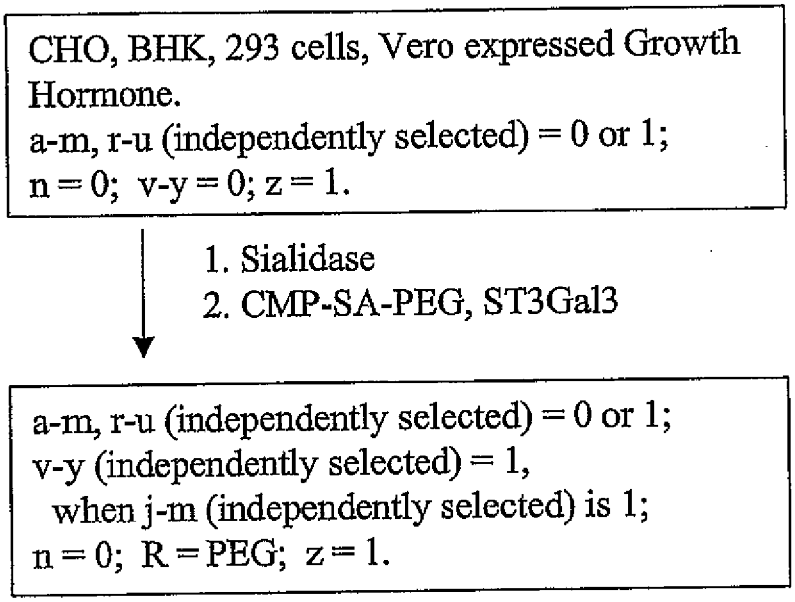

CHO, BHK, 293 cells, Vero expressed Growth Hormone.
a-m, r-u (independently selected) = 0 or 1;
n = 0; v-y = 0; z = 1.
1. Sialidase
2. CMP-SA-PEG, ST3Gal3
a-m, r-u (independently selected) = 0 or 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
n = 0; R = PEG; z = 1.

FIG. 45B

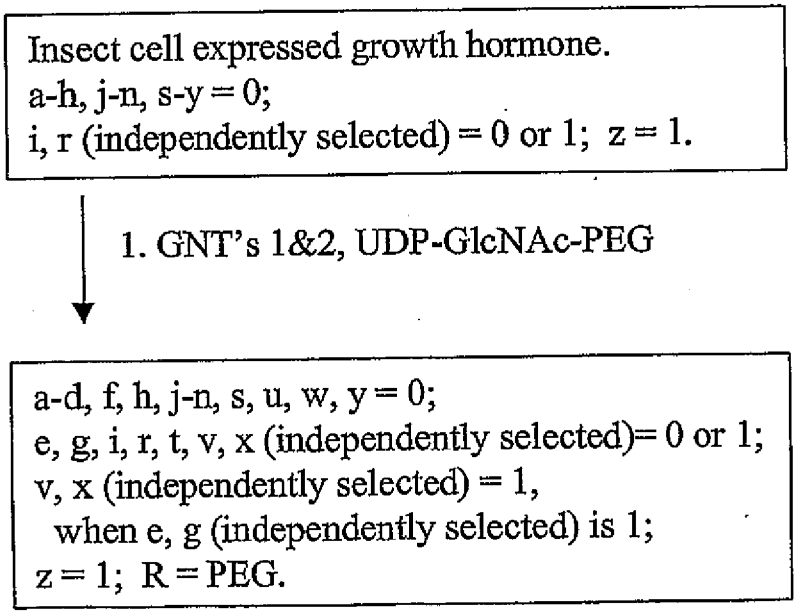
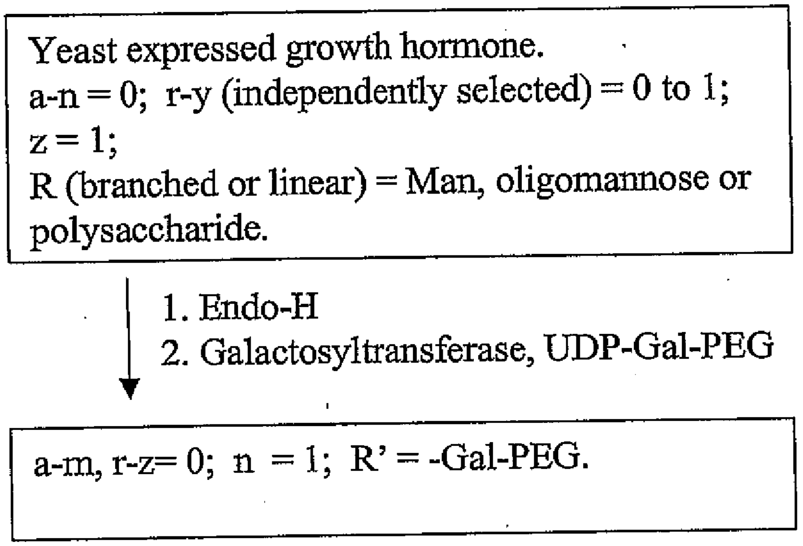

Insect cell expressed growth hormone.
a-h, j-n, s-y = 0;
i, r (independently selected) = 0 or 1; z = 1.
1. GNT's 1&2, UDP-GlcNAc-PEG
a-d, f, h, j-n, s, u, w, y = 0;
e, g, i, r, t, v, x (independently selected)= 0 or 1;
v, x (independently selected) = 1,
when e, g (independently selected) is 1;
z = 1; R = PEG.

FIG. 45C

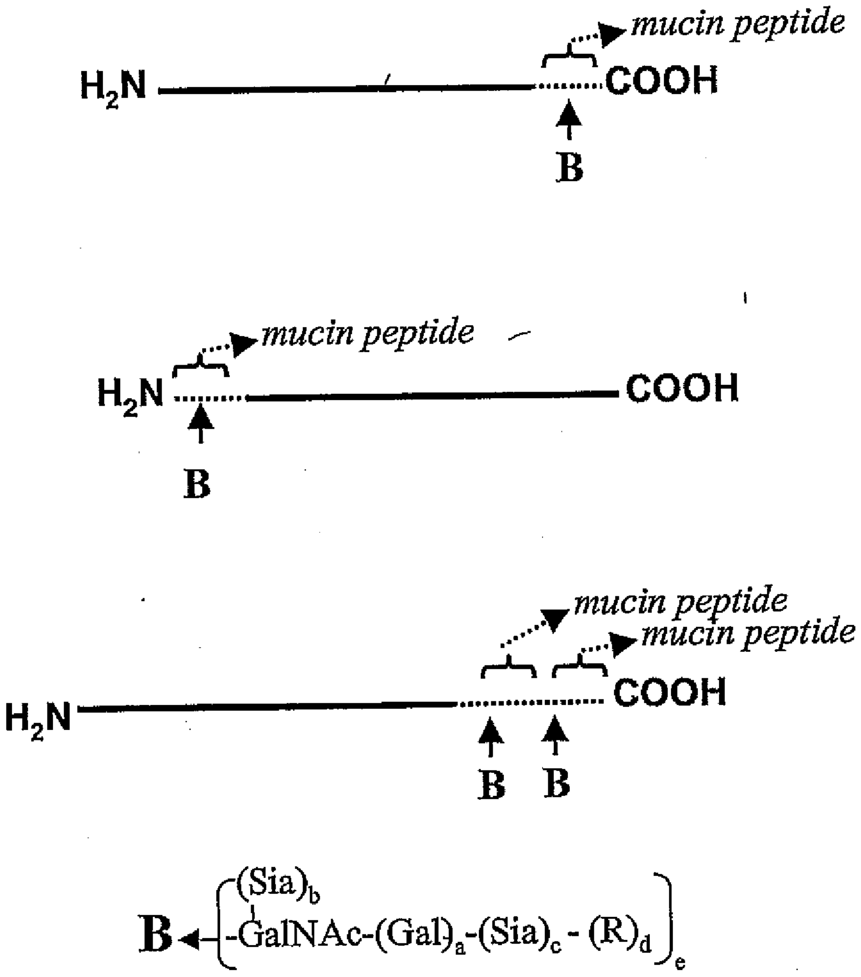


Yeast expressed growth hormone.
a-n = 0; r-y (independently selected) = 0 to 1;
z = 1;
R (branched or linear) = Man, oligomannose or polysaccharide.

1. Endo-H
2. Galactosyltransferase, UDP-Gal-PEG

a-m, r-z= 0; n = 1; R' = -Gal-PEG.

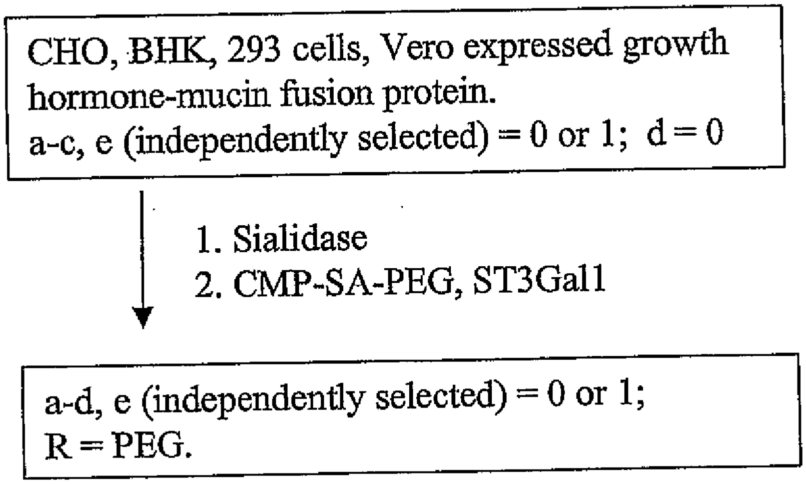
FIG. 45D



$$\mathbf{B} \leftarrow \left[\begin{array}{l} (\mathrm{Sia})_b \\ -\mathrm{GalNAc}\text{-}(\mathrm{Gal})_a\text{-}(\mathrm{Sia})_c\text{-}(\mathrm{R})_d \end{array} \right]_e$$

a-c, e (independently selected) = 0 or 1;
d = 0;
R = modifying group, mannose, oligomannose.

FIG. 45E

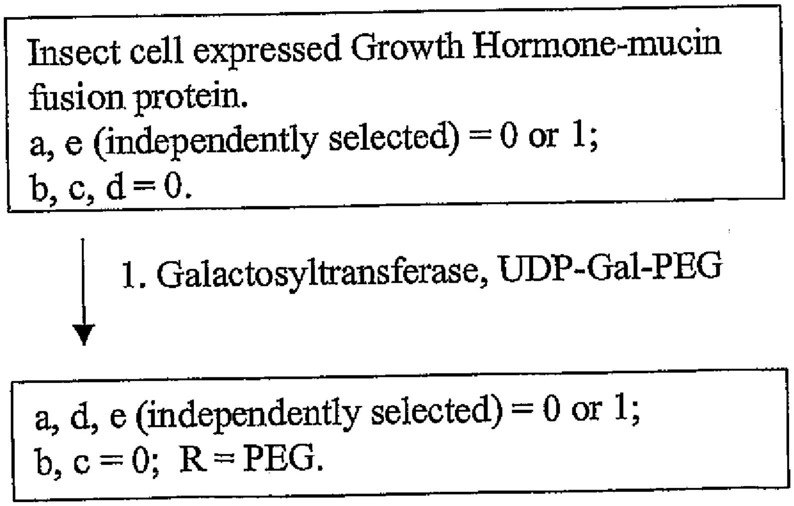


CHO, BHK, 293 cells, Vero expressed growth hormone-mucin fusion protein.
a-c, e (independently selected) = 0 or 1; d = 0

1. Sialidase
2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1;
R = PEG.

FIG. 45F



Insect cell expressed Growth Hormone-mucin fusion protein.
a, e (independently selected) = 0 or 1;
b, c, d = 0.

1. Galactosyltransferase, UDP-Gal-PEG

a, d, e (independently selected) = 0 or 1;
b, c = 0; R = PEG.

FIG. 45G

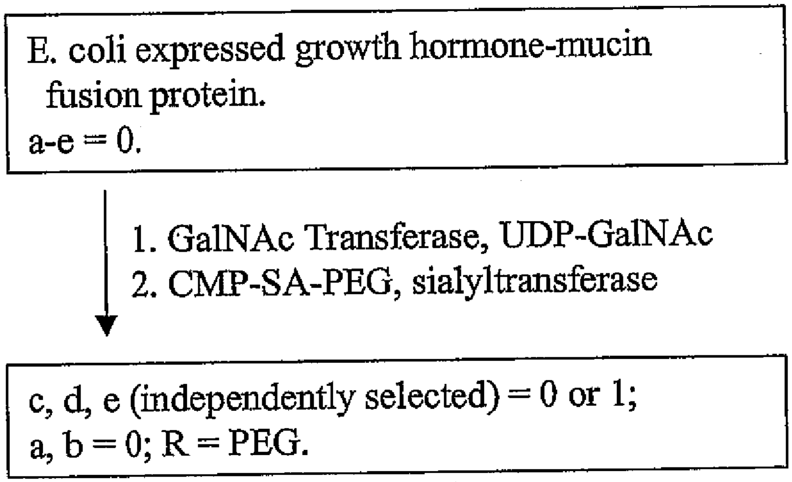

E. coli expressed growth hormone-mucin fusion protein.
a-e = 0.
1. GalNAc Transferase, UDP-GalNAc
2. CMP-SA-PEG, sialyltransferase
c, d, e (independently selected) = 0 or 1;
a, b = 0; R = PEG.

FIG. 45H

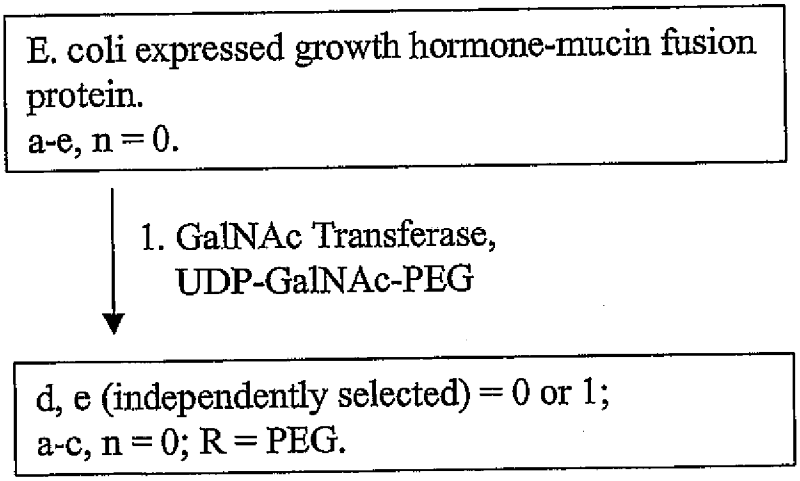

E. coli expressed growth hormone-mucin fusion protein.
a-e, n = 0.
1. GalNAc Transferase, UDP-GalNAc-PEG
d, e (independently selected) = 0 or 1;
a-c, n = 0; R = PEG.

FIG. 45I

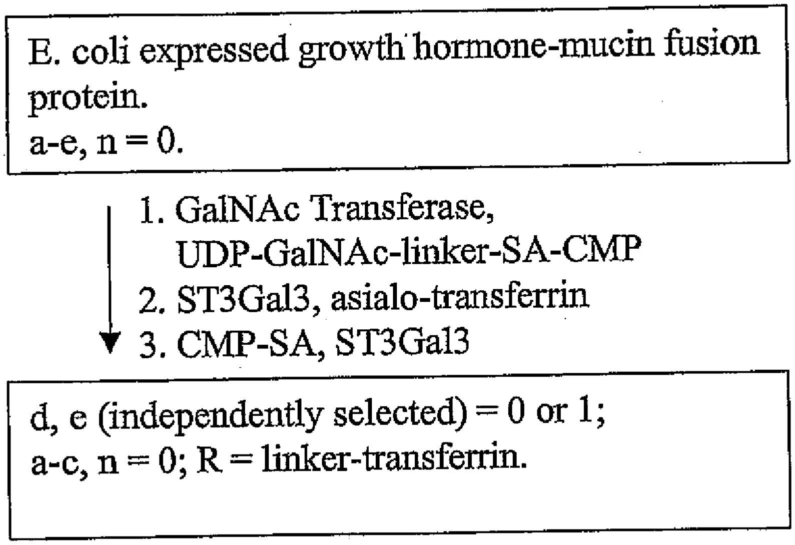

E. coli expressed growth hormone-mucin fusion protein.
a-e, n = 0.
1. GalNAc Transferase, UDP-GalNAc-linker-SA-CMP
2. ST3Gal3, asialo-transferrin
3. CMP-SA, ST3Gal3
d, e (independently selected) = 0 or 1;
a-c, n = 0; R = linker-transferrin.

FIG. 45J

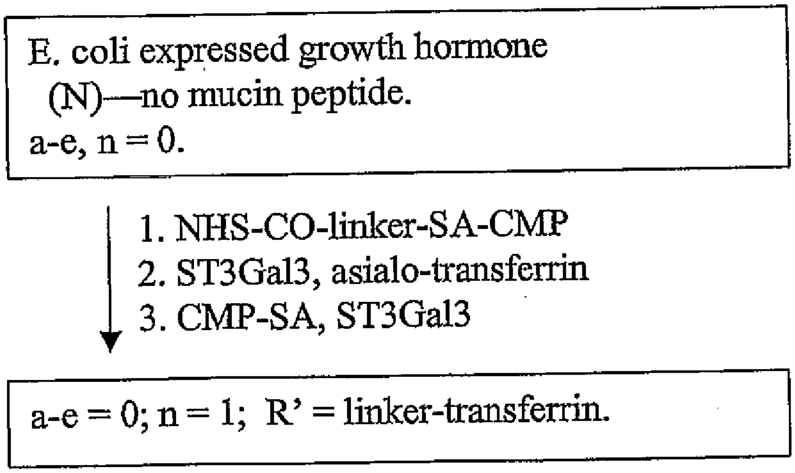
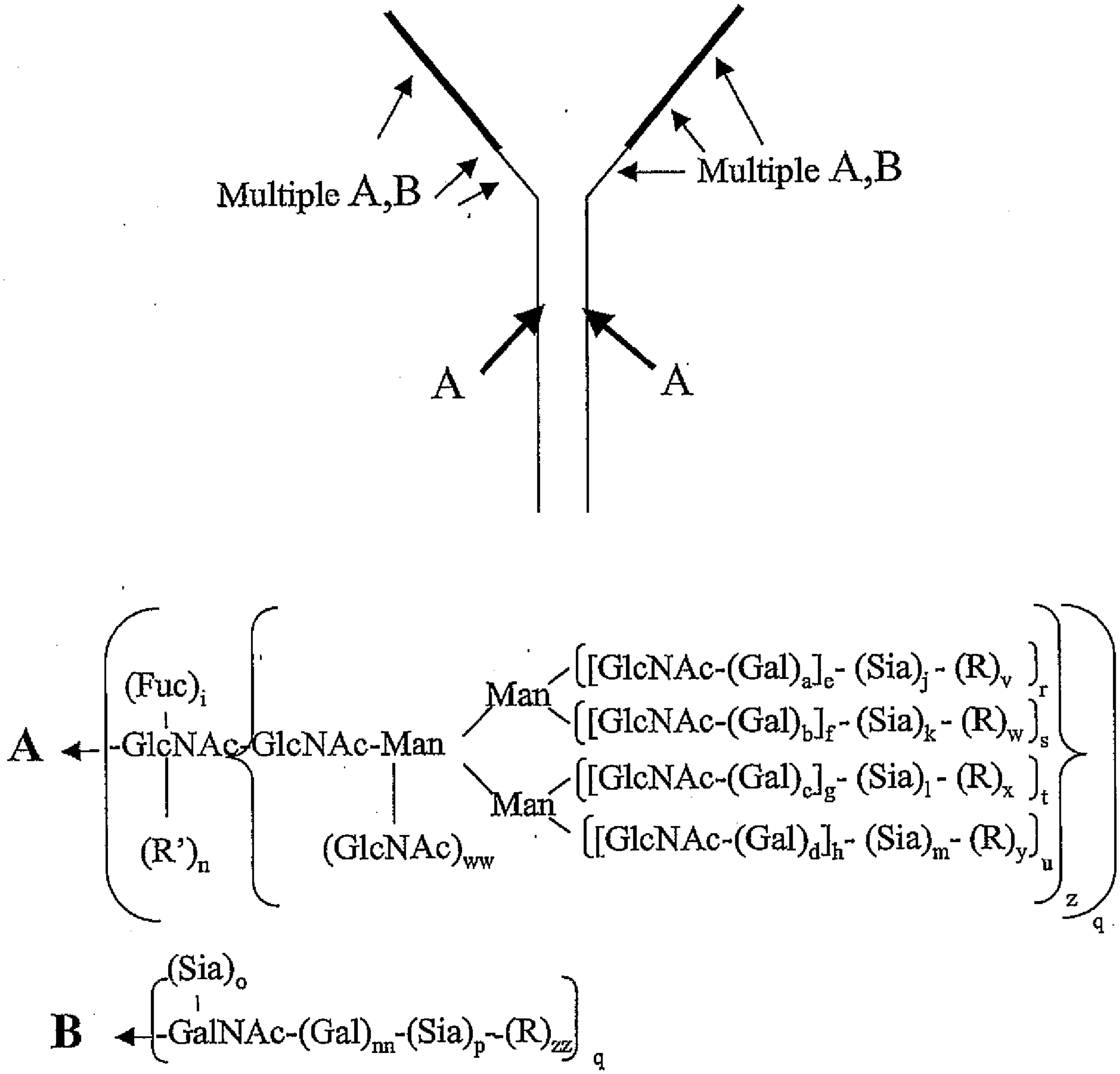

E. coli expressed growth hormone
(N)—no mucin peptide.
a-e, n = 0.
1. NHS-CO-linker-SA-CMP
2. ST3Gal3, asialo-transferrin
3. CMP-SA, ST3Gal3
a-e = 0; n = 1; R' = linker-transferrin.

FIG. 45K


Multiple A,B
Multiple A,B
A
A
A
(Fuc)$_i$
-GlcNAc-GlcNAc-Man
(R')$_n$
(GlcNAc)$_{ww}$
Man
Man
[[GlcNAc-(Gal)$_a$]$_e$- (Sia)$_j$ - (R)$_v$]$_r$
[[GlcNAc-(Gal)$_b$]$_f$- (Sia)$_k$ - (R)$_w$]$_s$
[[GlcNAc-(Gal)$_c$]$_g$- (Sia)$_l$ - (R)$_x$]$_t$
[[GlcNAc-(Gal)$_d$]$_h$- (Sia)$_m$ - (R)$_y$]$_u$
z
q
B
(Sia)$_o$
-GalNAc-(Gal)$_{nn}$-(Sia)$_p$-(R)$_{zz}$
q

a-d, i-m, q-u, w, z, nn, ww, zz (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
n, v-y = 0;
R = modifying group, mannose, oligo-mannose;
R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 46A

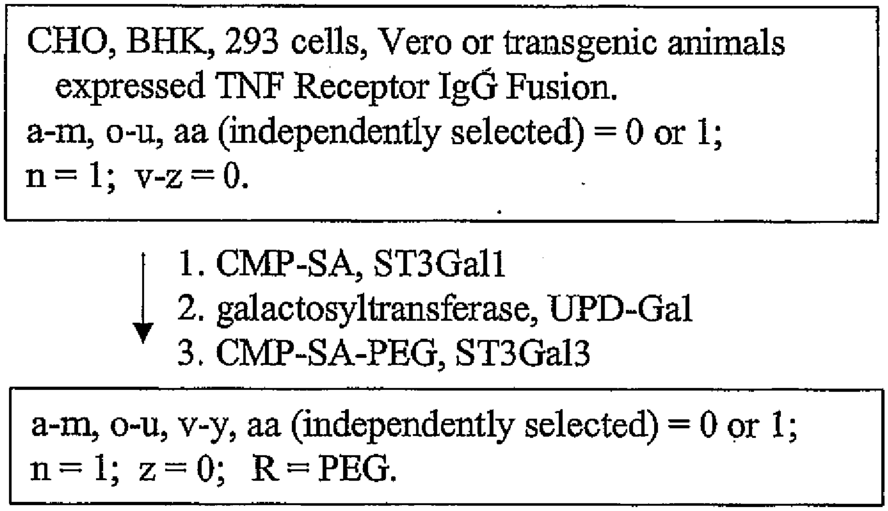

CHO, BHK, 293 cells, Vero or transgenic animals expressed TNF Receptor IgG Fusion.
a-m, o-u, aa (independently selected) = 0 or 1;
n = 1; v-z = 0.
1. CMP-SA, ST3Gal1
2. galactosyltransferase, UPD-Gal
3. CMP-SA-PEG, ST3Gal3
a-m, o-u, v-y, aa (independently selected) = 0 or 1;
n = 1; z = 0; R = PEG.

FIG. 46B

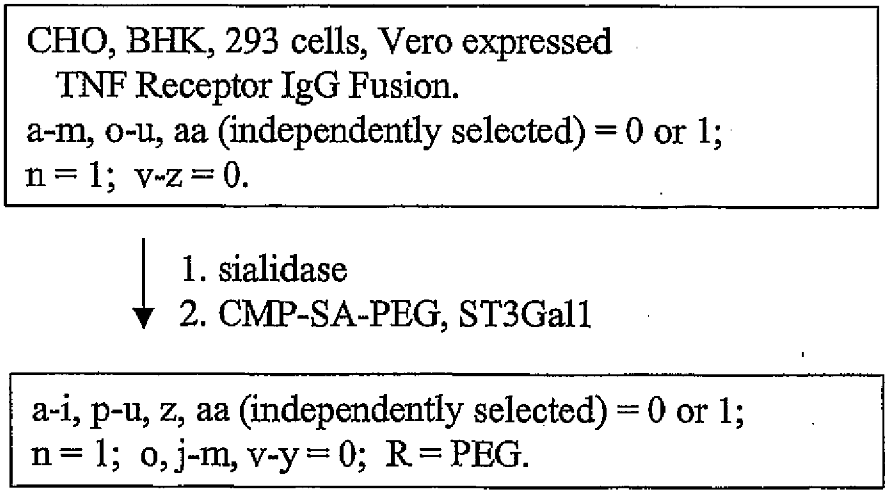

CHO, BHK, 293 cells, Vero expressed TNF Receptor IgG Fusion.
a-m, o-u, aa (independently selected) = 0 or 1;
n = 1; v-z = 0.
1. sialidase
2. CMP-SA-PEG, ST3Gal1
a-i, p-u, z, aa (independently selected) = 0 or 1;
n = 1; o, j-m, v-y = 0; R = PEG.

FIG. 46C

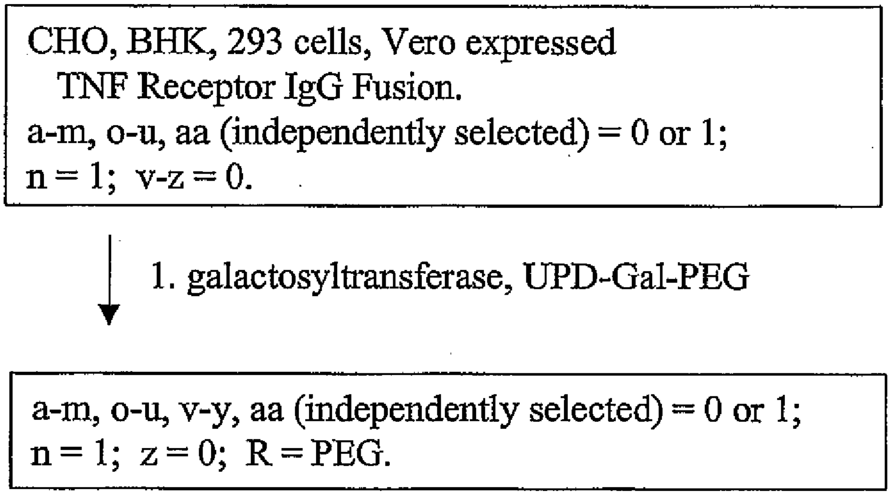

CHO, BHK, 293 cells, Vero expressed TNF Receptor IgG Fusion.
a-m, o-u, aa (independently selected) = 0 or 1;
n = 1; v-z = 0.
1. galactosyltransferase, UPD-Gal-PEG
a-m, o-u, v-y, aa (independently selected) = 0 or 1;
n = 1; z = 0; R = PEG.

FIG. 46D

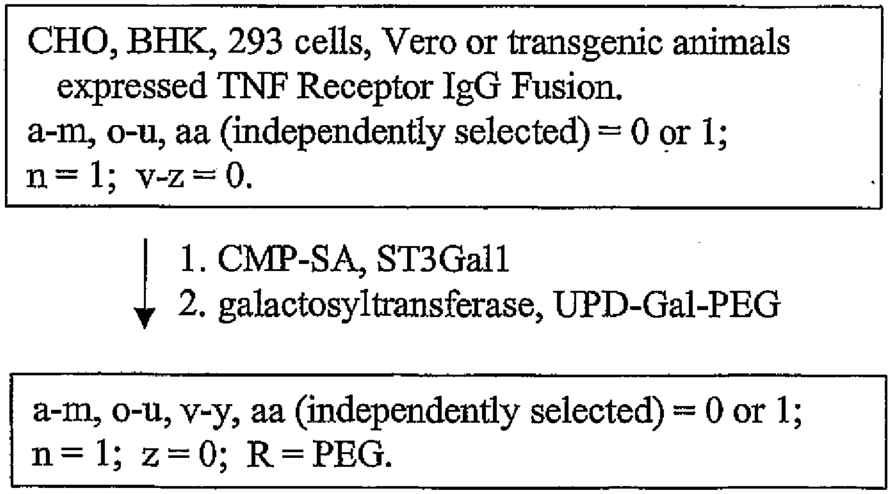

CHO, BHK, 293 cells, Vero or transgenic animals expressed TNF Receptor IgG Fusion.
a-m, o-u, aa (independently selected) = 0 or 1;
n = 1; v-z = 0.
1. CMP-SA, ST3Gal1
2. galactosyltransferase, UPD-Gal-PEG
a-m, o-u, v-y, aa (independently selected) = 0 or 1;
n = 1; z = 0; R = PEG.

FIG. 46E

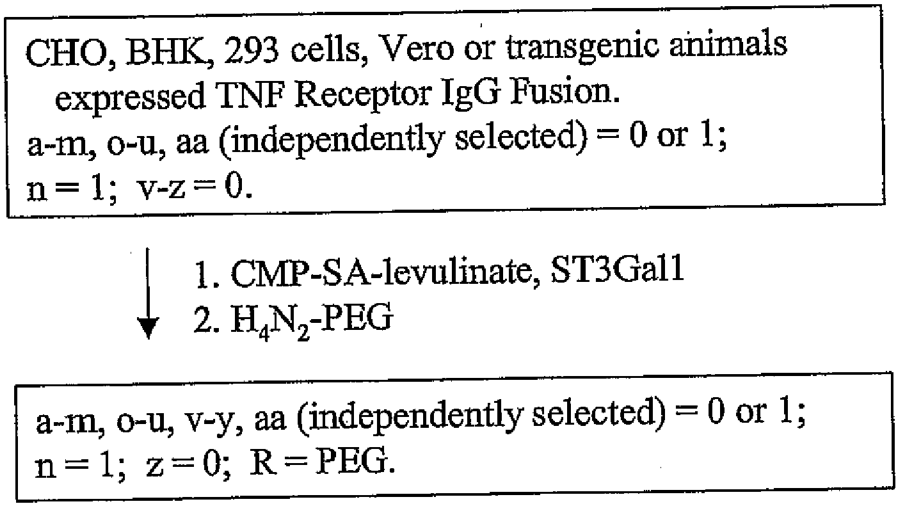

CHO, BHK, 293 cells, Vero or transgenic animals expressed TNF Receptor IgG Fusion.
a-m, o-u, aa (independently selected) = 0 or 1;
n = 1; v-z = 0.
1. CMP-SA-levulinate, ST3Gal1
2. H_4N_2-PEG
a-m, o-u, v-y, aa (independently selected) = 0 or 1;
n = 1; z = 0; R = PEG.

FIG. 46F

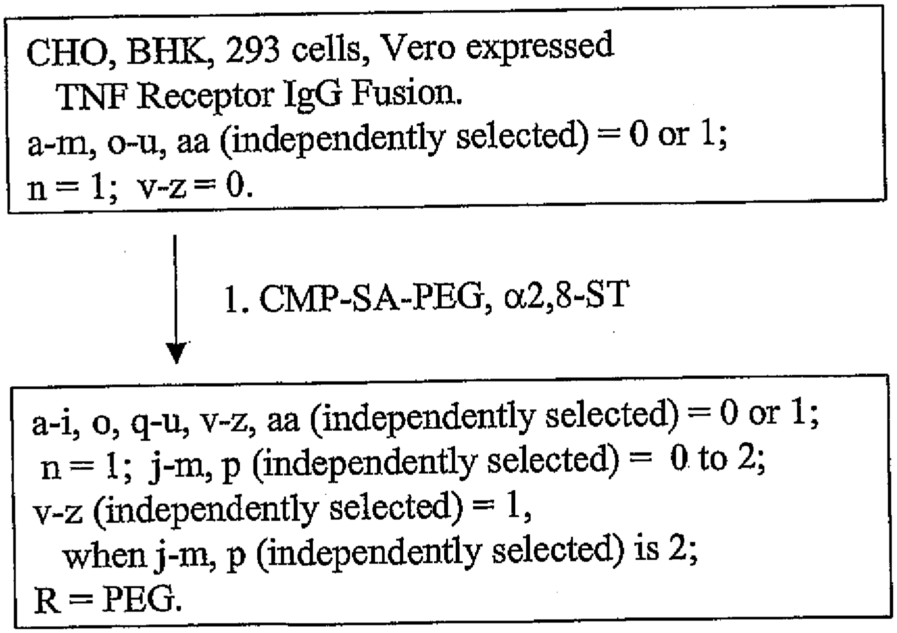
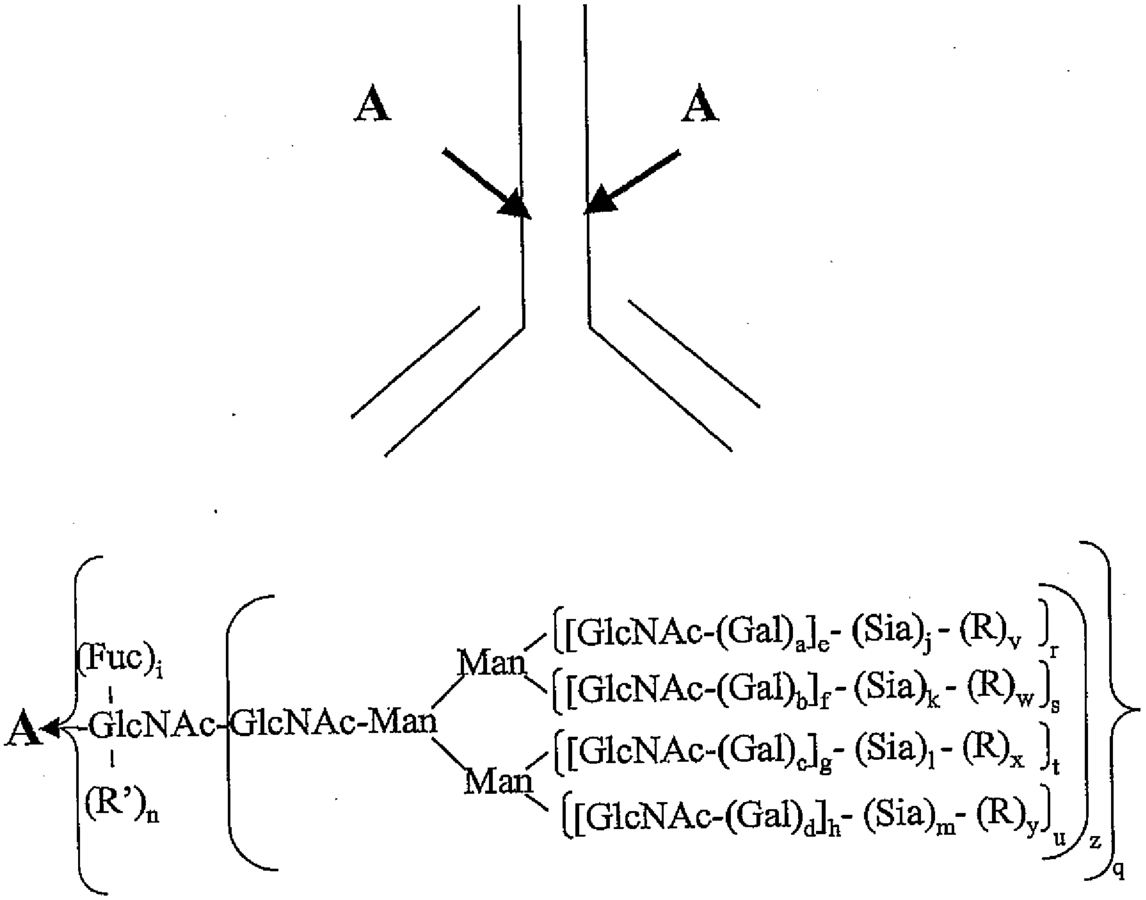
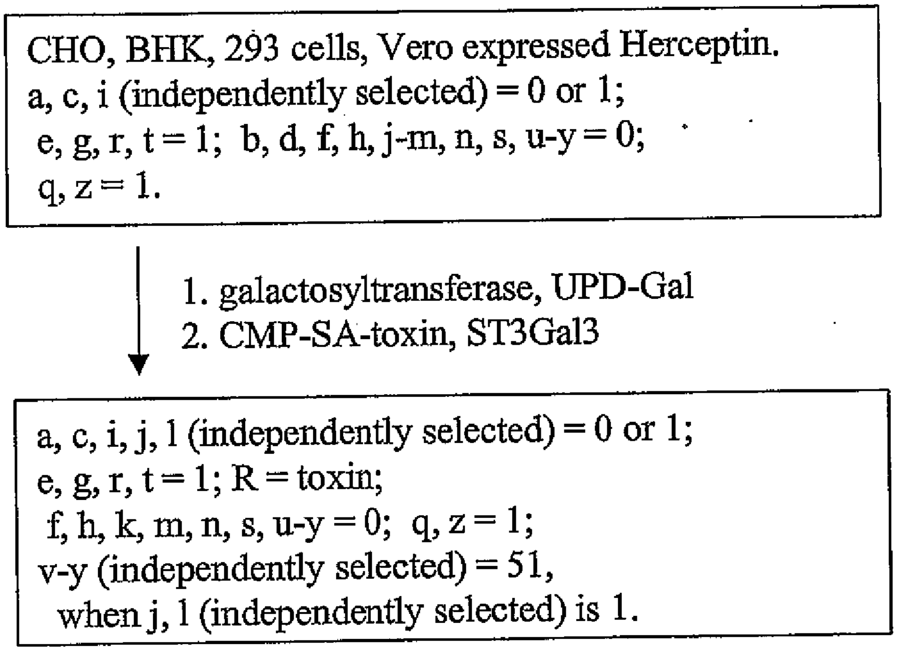

CHO, BHK, 293 cells, Vero expressed TNF Receptor IgG Fusion.
a-m, o-u, aa (independently selected) = 0 or 1;
n = 1; v-z = 0.
1. CMP-SA-PEG, α2,8-ST
a-i, o, q-u, v-z, aa (independently selected) = 0 or 1;
n = 1; j-m, p (independently selected) = 0 to 2;
v-z (independently selected) = 1,
when j-m, p (independently selected) is 2;
R = PEG.

FIG. 46G


A
A
(Fuc)$_i$
A←-GlcNAc-GlcNAc-Man
(R')$_n$
Man
Man
[[GlcNAc-(Gal)$_a$]$_e$- (Sia)$_j$ - (R)$_v$]$_r$
[[GlcNAc-(Gal)$_b$]$_f$- (Sia)$_k$ - (R)$_w$]$_s$
[[GlcNAc-(Gal)$_c$]$_g$- (Sia)$_l$ - (R)$_x$]$_t$
[[GlcNAc-(Gal)$_d$]$_h$- (Sia)$_m$- (R)$_y$]$_u$
z
q

a-d, i, l, q-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
j-k (independently selected) = 0 or 1.
M = 0 to 20.
n, v-y = 0; z = 0 or 1;
R = polymer, toxin, radioisotope-complex, drug, mannose, oligo-mannose.
R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 47A

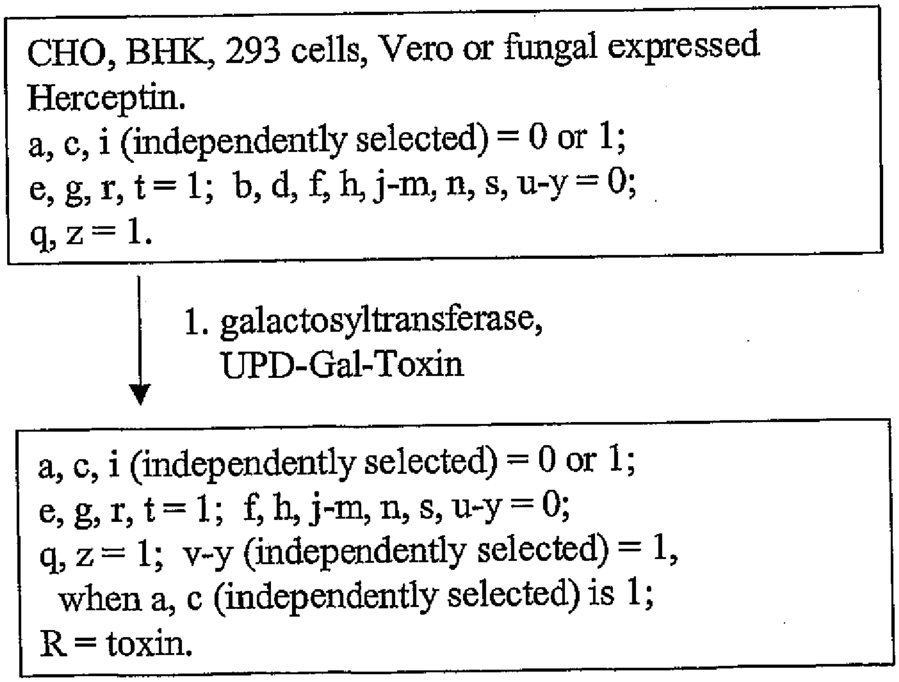


CHO, BHK, 293 cells, Vero expressed Herceptin.
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;
q, z = 1.

1. galactosyltransferase, UPD-Gal
2. CMP-SA-toxin, ST3Gal3

a, c, i, j, l (independently selected) = 0 or 1;
e, g, r, t = 1; R = toxin;
f, h, k, m, n, s, u-y = 0; q, z = 1;
v-y (independently selected) = 51,
when j, l (independently selected) is 1.

FIG. 47B



CHO, BHK, 293 cells, Vero or fungal expressed Herceptin.
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;
q, z = 1.

1. galactosyltransferase, UPD-Gal-Toxin

a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, j-m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when a, c (independently selected) is 1;
R = toxin.

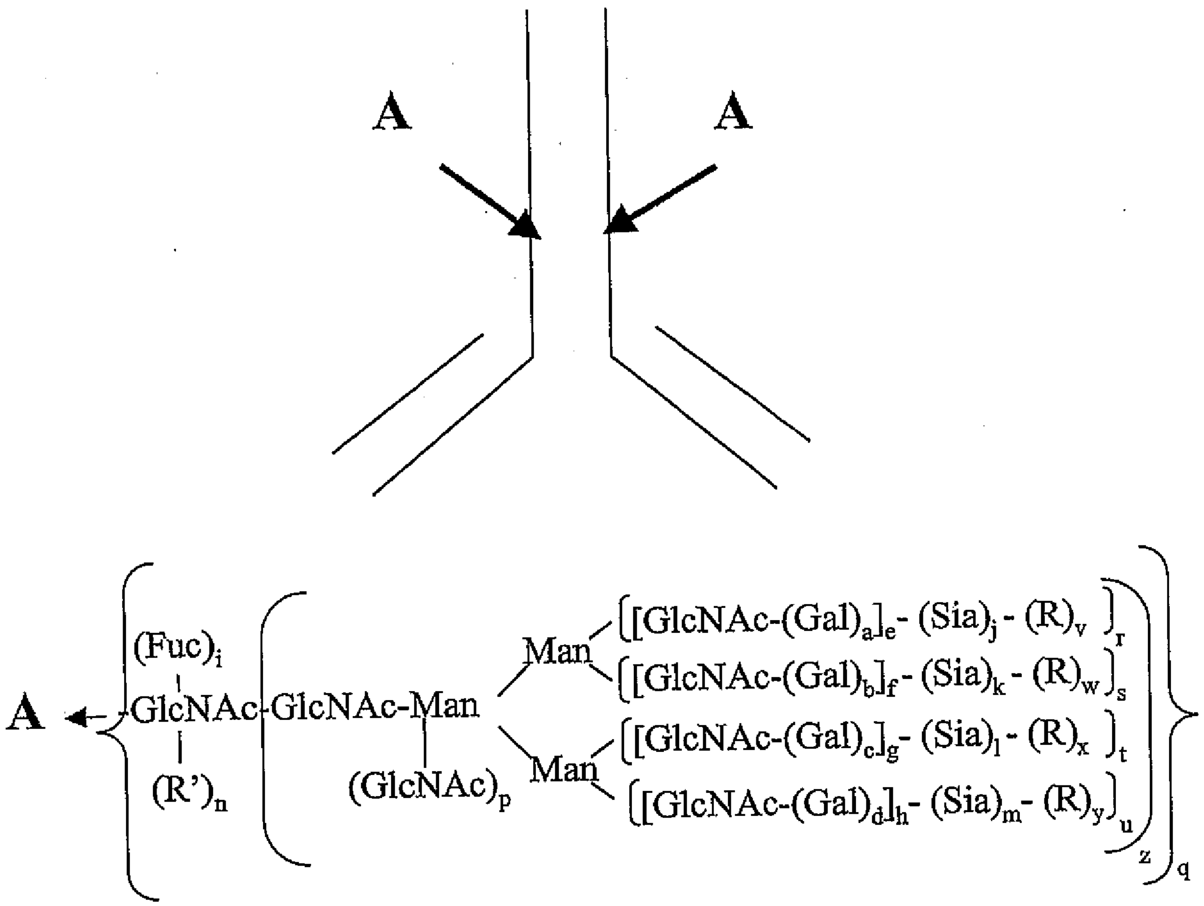
FIG. 47C

Fungi expressed Herceptin.
e, g, i, r, t (independently selected) = 0 or 1;
a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.

↓
1. Endo-H
2. Galactosyltransferase, UDP-Gal
3.. CMP-SA-radioisotope complex, ST3Gal3

a-m, r-z= 0; q, n = 1;
R' = -Gal-Sia-radioisotope complex.

FIG. 47D


A
A
A
(Fuc)$_i$
GlcNAc-GlcNAc-Man
(R')$_n$
(GlcNAc)$_p$
Man
Man
[[GlcNAc-(Gal)$_a$]$_e$- (Sia)$_j$ - (R)$_v$]$_r$
[[GlcNAc-(Gal)$_b$]$_f$- (Sia)$_k$ - (R)$_w$]$_s$
[[GlcNAc-(Gal)$_c$]$_g$- (Sia)$_l$ - (R)$_x$]$_t$
[[GlcNAc-(Gal)$_d$]$_h$- (Sia)$_m$- (R)$_y$]$_u$
z
q

a-d, i, p-u, (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
j-m (independently selected) = 0 or 1.
n, v-y = 0; z = 0 or 1;
R = polymer, toxin, radioisotope-complex, drug, mannose, oligo-mannose.
R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 48A

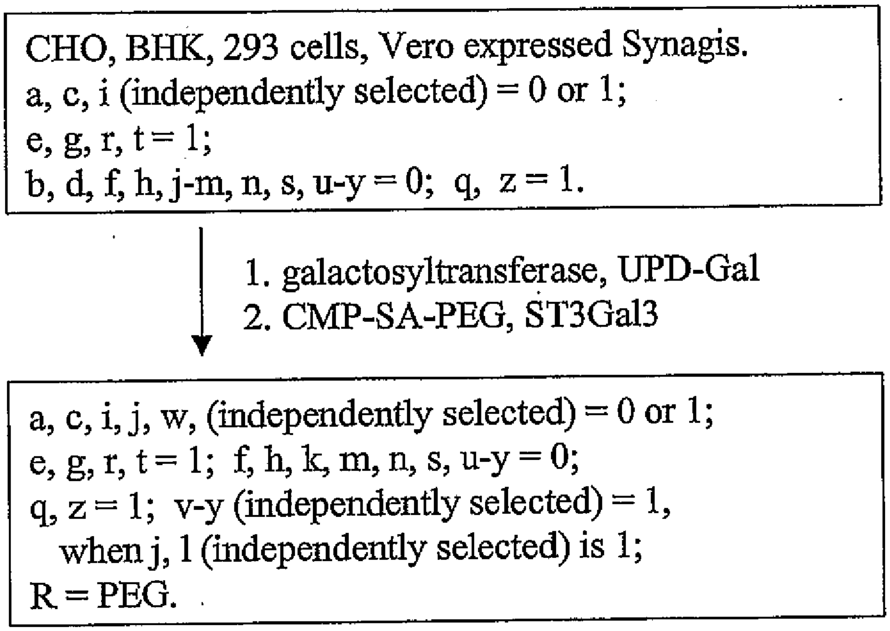

CHO, BHK, 293 cells, Vero expressed Synagis.
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1;
b, d, f, h, j-m, n, s, u-y = 0; q, z = 1.
1. galactosyltransferase, UPD-Gal
2. CMP-SA-PEG, ST3Gal3
a, c, i, j, w, (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, k, m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when j, l (independently selected) is 1;
R = PEG.

FIG. 48B

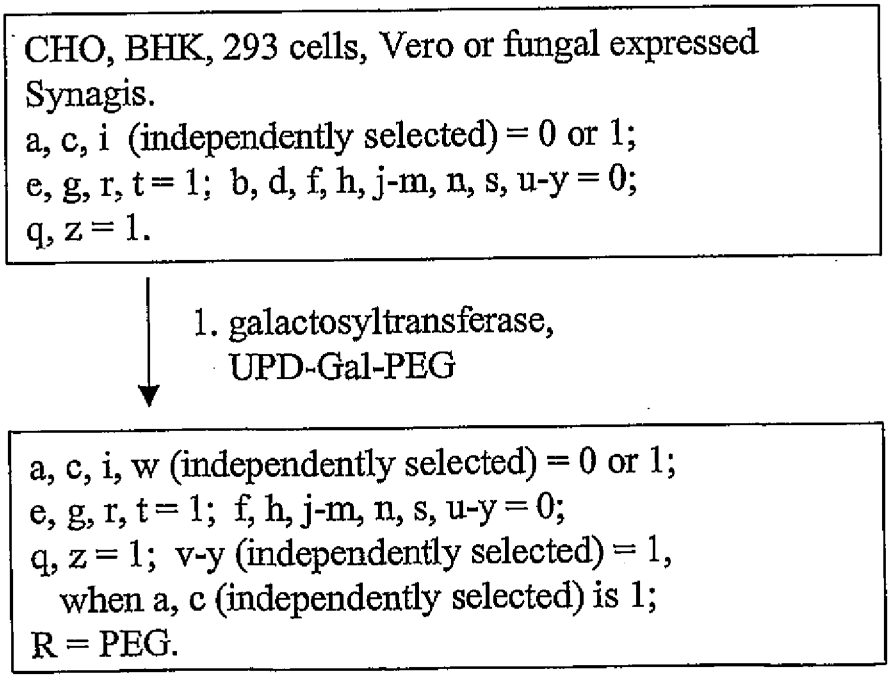

CHO, BHK, 293 cells, Vero or fungal expressed Synagis.
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;
q, z = 1.
1. galactosyltransferase, UPD-Gal-PEG
a, c, i, w (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, j-m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when a, c (independently selected) is 1;
R = PEG.

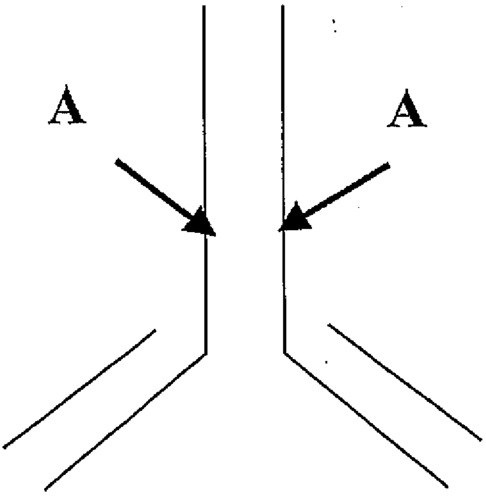
FIG. 48C

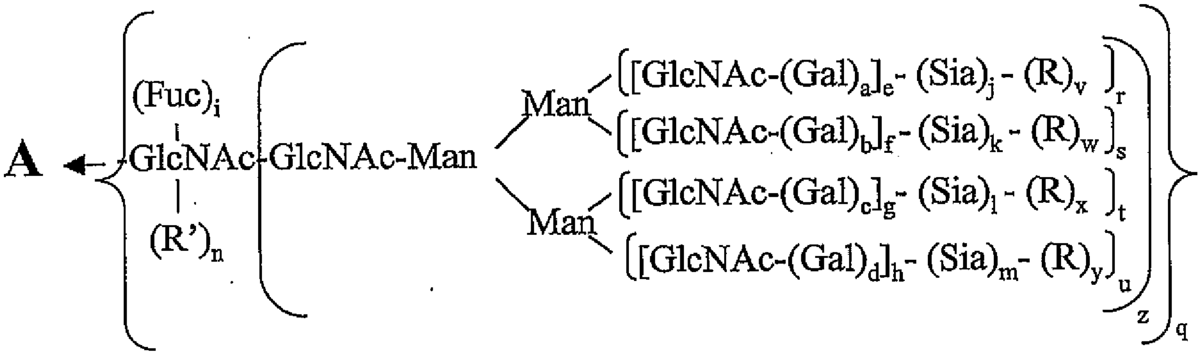
Fungi expressed Synagis.
e, g, i, r, t (independently selected) = 0 or 1;
a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.

1. Endo-H
2. Galactosyltransferase, UDP-Gal
3.. CMP-SA-PEG, ST3Gal3

a-m, r-z= 0; q, n = 1; R' = -Gal-Sia-PEG.

FIG. 48D





$$\mathbf{A} \leftarrow \left\{ \begin{array}{c} (\mathrm{Fuc})_i \\ | \\ \mathrm{GlcNAc} \\ | \\ (\mathrm{R'})_n \end{array} - \left(\mathrm{GlcNAc\text{-}Man} \begin{array}{l} \diagup \mathrm{Man} \begin{array}{l} \diagup \left([\mathrm{GlcNAc\text{-}(Gal)}_a]_e\text{-}(\mathrm{Sia})_j\text{-}(\mathrm{R})_v \right)_r \\ \diagdown \left([\mathrm{GlcNAc\text{-}(Gal)}_b]_f\text{-}(\mathrm{Sia})_k\text{-}(\mathrm{R})_w \right)_s \end{array} \\ \diagdown \mathrm{Man} \begin{array}{l} \diagup \left([\mathrm{GlcNAc\text{-}(Gal)}_c]_g\text{-}(\mathrm{Sia})_l\text{-}(\mathrm{R})_x \right)_t \\ \diagdown \left([\mathrm{GlcNAc\text{-}(Gal)}_d]_h\text{-}(\mathrm{Sia})_m\text{-}(\mathrm{R})_y \right)_u \end{array} \end{array} \right)_z \right\}_q$$

a-d, i, q-u, w (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 20.
n, v-y = 0; z = 0 or 1;
R = polymer, toxin, radioisotope-complex, drug, mannose, oligo-mannose.
R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 49A

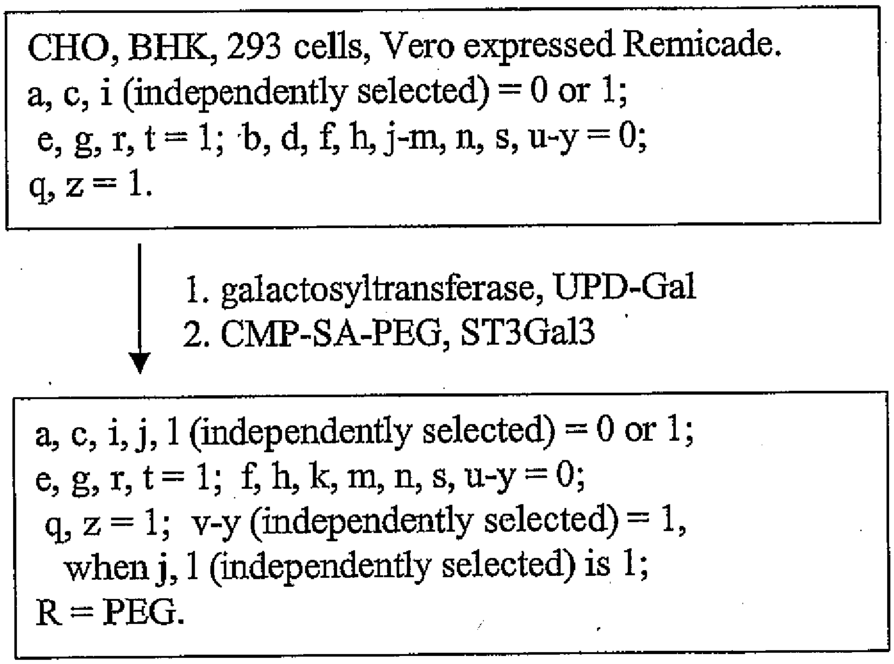

CHO, BHK, 293 cells, Vero expressed Remicade.
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;
q, z = 1.
1. galactosyltransferase, UPD-Gal
2. CMP-SA-PEG, ST3Gal3
a, c, i, j, 1 (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, k, m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when j, 1 (independently selected) is 1;
R = PEG.

FIG. 49B

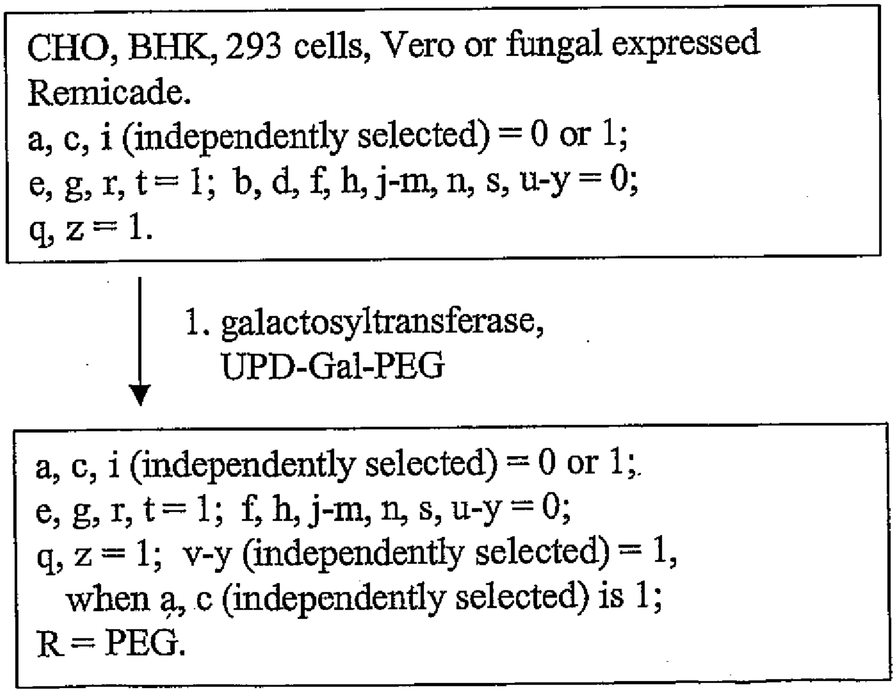

CHO, BHK, 293 cells, Vero or fungal expressed Remicade.
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;
q, z = 1.
1. galactosyltransferase, UPD-Gal-PEG
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, j-m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when a, c (independently selected) is 1;
R = PEG.

FIG. 49C

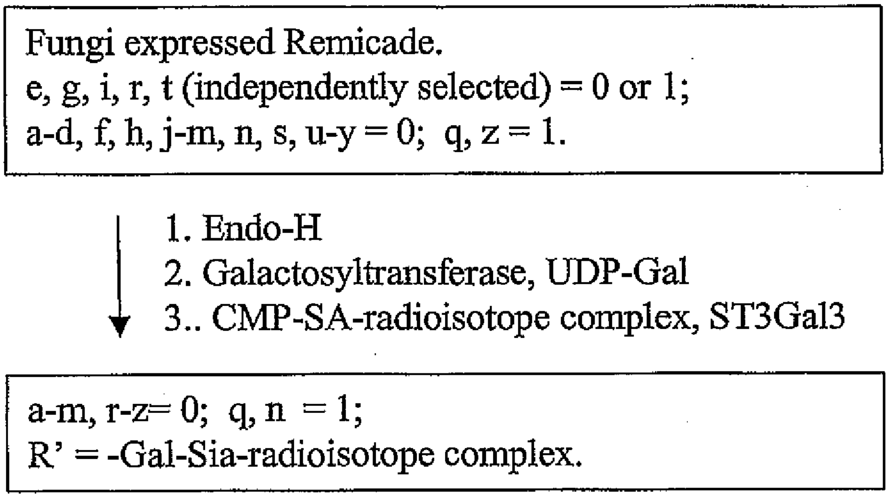
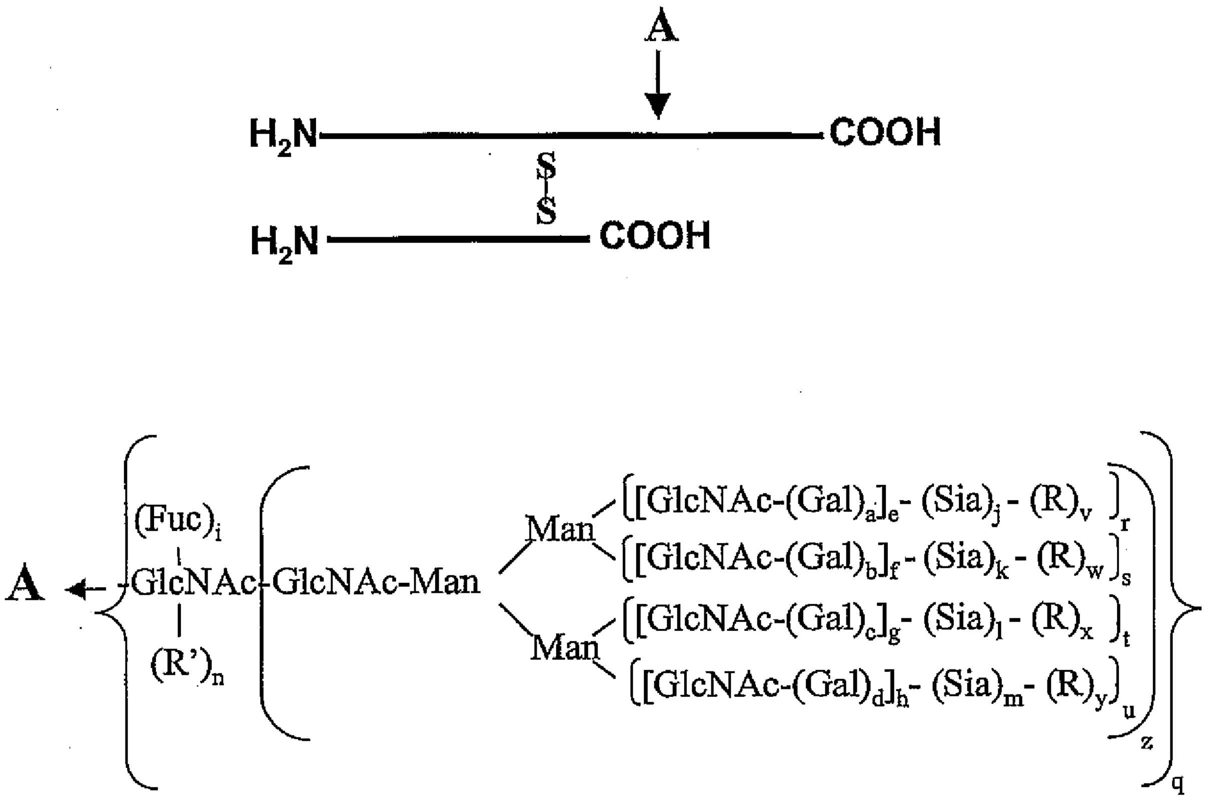

Fungi expressed Remicade.
e, g, i, r, t (independently selected) = 0 or 1;
a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.
1. Endo-H
2. Galactosyltransferase, UDP-Gal
3.. CMP-SA-radioisotope complex, ST3Gal3
a-m, r-z= 0; q, n = 1;
R' = -Gal-Sia-radioisotope complex.

FIG. 49D


A
H2N
COOH
S
S
H2N
COOH
A
(Fuc)i
GlcNAc
GlcNAc-Man
(R')n
Man
Man
[[GlcNAc-(Gal)a]e- (Sia)j - (R)v]r
[[GlcNAc-(Gal)b]f - (Sia)k - (R)w]s
[[GlcNAc-(Gal)c]g- (Sia)l - (R)x]t
[[GlcNAc-(Gal)d]h- (Sia)m- (R)y]u
z
q

a-d, i, q-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
j-m (independently selected) = 0 or 1.
n, v-y = 0; z = 0 or 1;
R = modifying group, mannose, oligo-mannose;
R' = H, glycosyl residue, modifying group,
glycoconjugate.

FIG. 50A

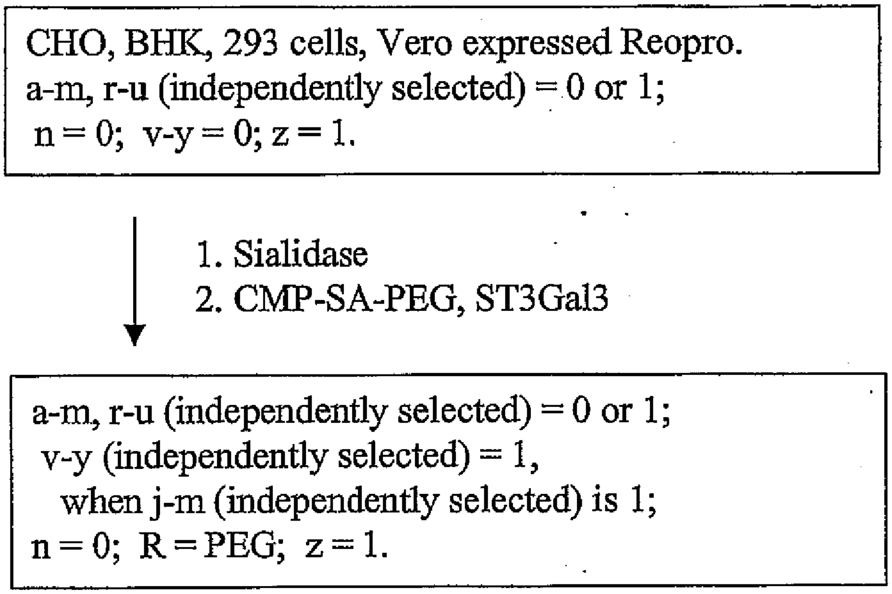

CHO, BHK, 293 cells, Vero expressed Reopro.
a-m, r-u (independently selected) = 0 or 1;
n = 0; v-y = 0; z = 1.
1. Sialidase
2. CMP-SA-PEG, ST3Gal3
a-m, r-u (independently selected) = 0 or 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
n = 0; R = PEG; z = 1.

FIG. 50B

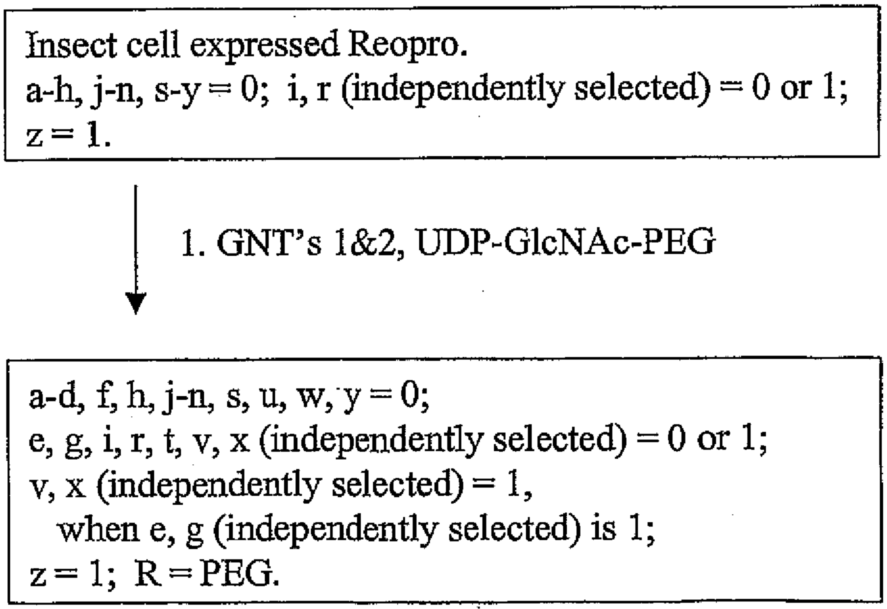

Insect cell expressed Reopro.
a-h, j-n, s-y = 0; i, r (independently selected) = 0 or 1;
z = 1.
1. GNT's 1&2, UDP-GlcNAc-PEG
a-d, f, h, j-n, s, u, w, y = 0;
e, g, i, r, t, v, x (independently selected) = 0 or 1;
v, x (independently selected) = 1,
when e, g (independently selected) is 1;
z = 1; R = PEG.

FIG. 50C

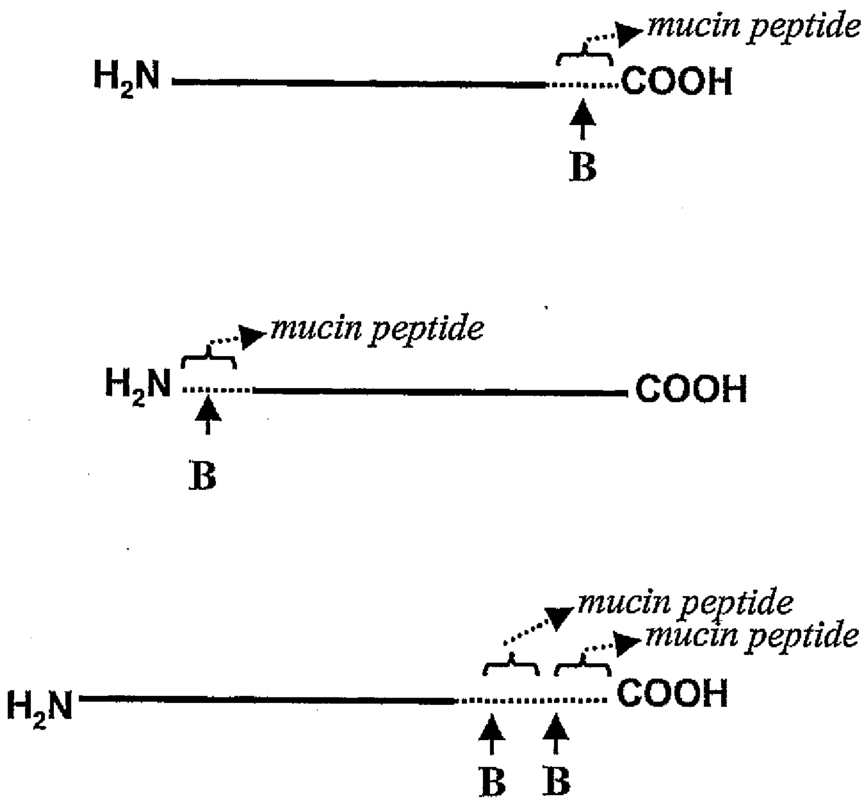
Yeast expressed Reopro.
a-n = 0; r-y (independently selected) = 0 to 1;
z = 1;
R (branched or linear) = Man, oligomannose or polysaccharide.

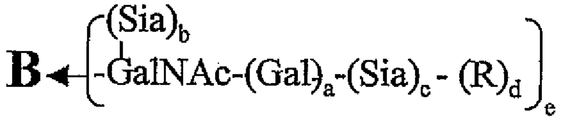
↓

1. Endo-H
2. Galactosyltransferase, UDP-Gal-PEG

a-m, r-z= 0; n = 1; R' = -Gal-PEG.

FIG. 50D





$$\mathbf{B} \leftarrow \left[\overset{(\mathrm{Sia})_b}{\overset{|}{\text{-GalNAc}}}\text{-}(\mathrm{Gal})_a\text{-}(\mathrm{Sia})_c\text{-}(\mathrm{R})_d \right]_e$$

a-c, e (independently selected) = 0 or 1;
d = 0; R = polymer

FIG. 50E

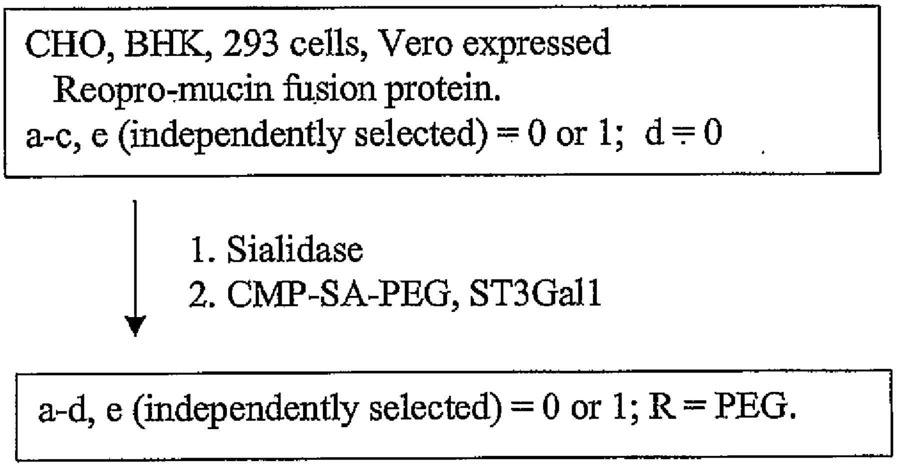

CHO, BHK, 293 cells, Vero expressed Reopro-mucin fusion protein.
a-c, e (independently selected) = 0 or 1; d = 0
1. Sialidase
2. CMP-SA-PEG, ST3Gal1
a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 50F

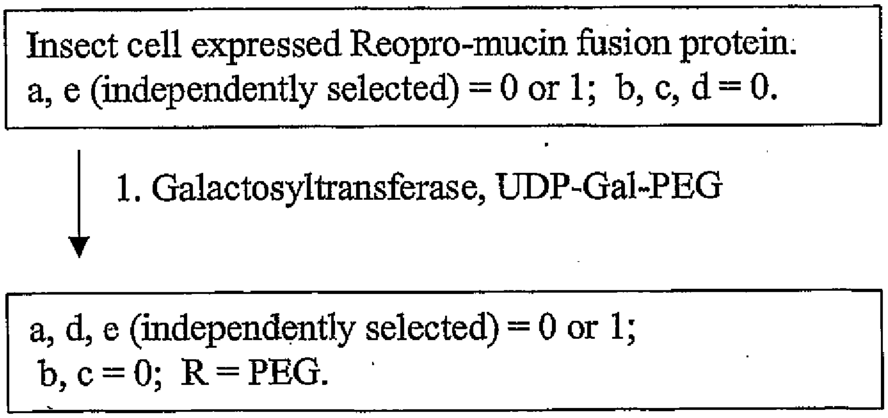

Insect cell expressed Reopro-mucin fusion protein.
a, e (independently selected) = 0 or 1; b, c, d = 0.
1. Galactosyltransferase, UDP-Gal-PEG
a, d, e (independently selected) = 0 or 1;
b, c = 0; R = PEG.

FIG. 50G

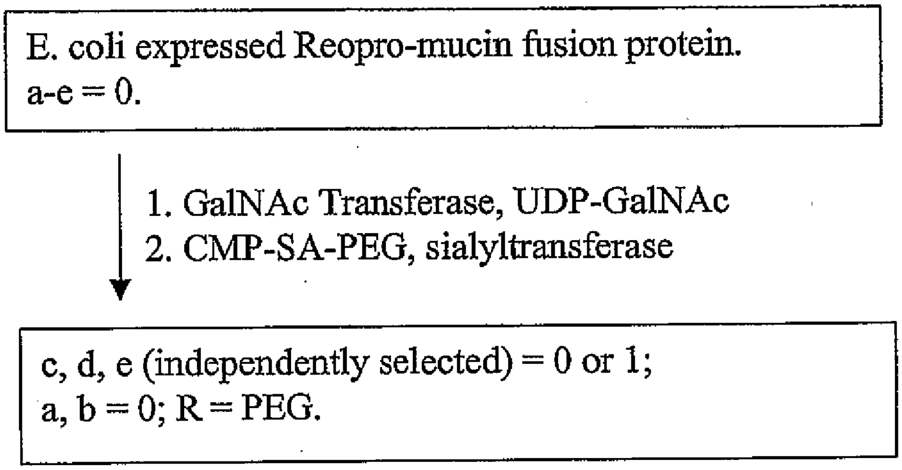
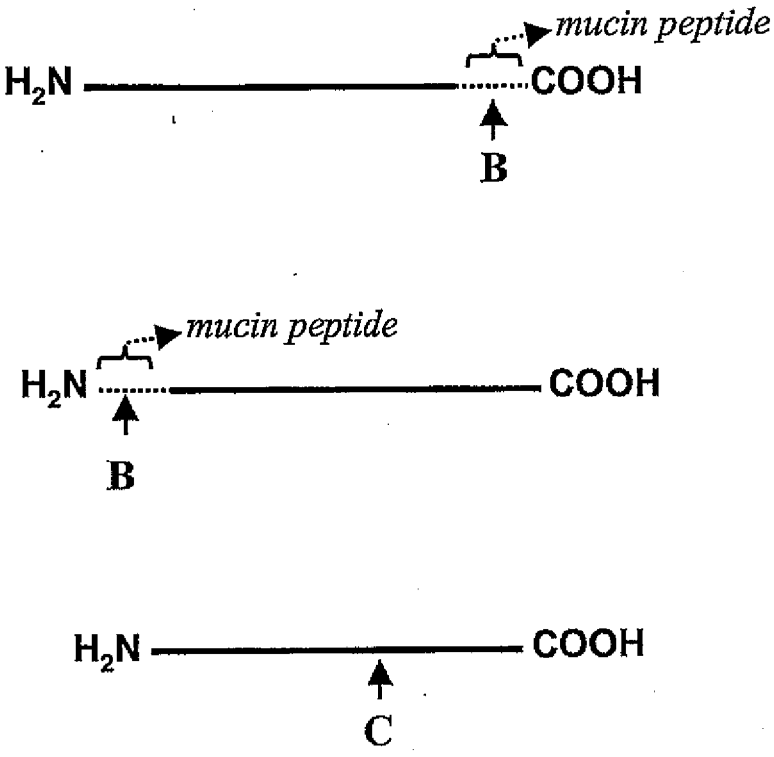
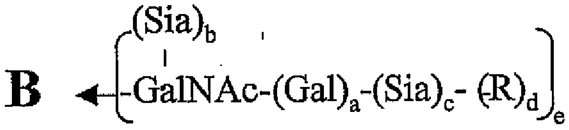

E. coli expressed Reopro-mucin fusion protein.
a-e = 0.
1. GalNAc Transferase, UDP-GalNAc
2. CMP-SA-PEG, sialyltransferase
c, d, e (independently selected) = 0 or 1;
a, b = 0; R = PEG.

FIG. 50H





$$\mathbf{B} \leftarrow \left[-\overset{(\mathrm{Sia})_b}{\mathrm{GalNAc}}-(\mathrm{Gal})_a-(\mathrm{Sia})_c-(\mathrm{R})_d \right]_e$$

$$\mathbf{C} \leftarrow (\mathrm{R'})_n$$

a-c, e (independently selected) = 0 or 1;
d = 0; R = polymer, linker.

FIG. 50I

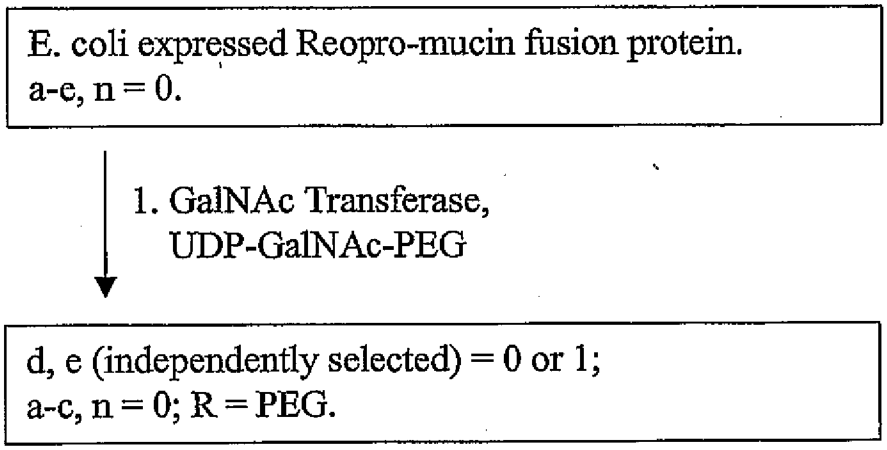

E. coli expressed Reopro-mucin fusion protein.
a-e, n = 0.
1. GalNAc Transferase,
UDP-GalNAc-PEG
d, e (independently selected) = 0 or 1;
a-c, n = 0; R = PEG.

FIG. 50J

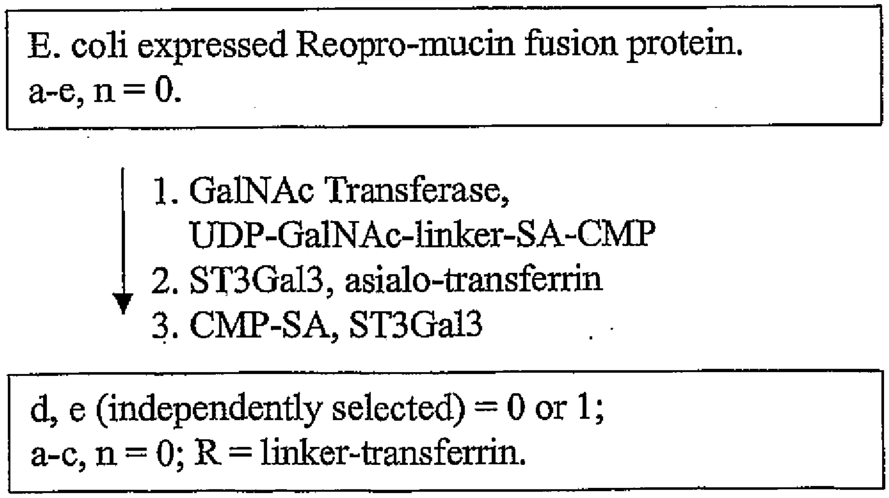

E. coli expressed Reopro-mucin fusion protein.
a-e, n = 0.
1. GalNAc Transferase,
UDP-GalNAc-linker-SA-CMP
2. ST3Gal3, asialo-transferrin
3. CMP-SA, ST3Gal3
d, e (independently selected) = 0 or 1;
a-c, n = 0; R = linker-transferrin.

FIG. 50K

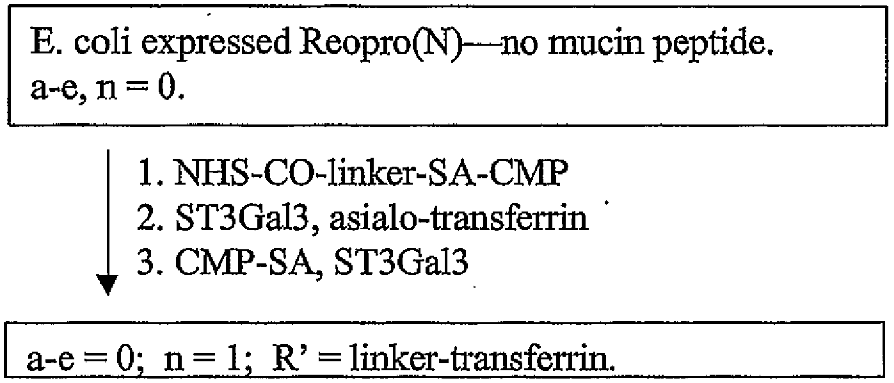
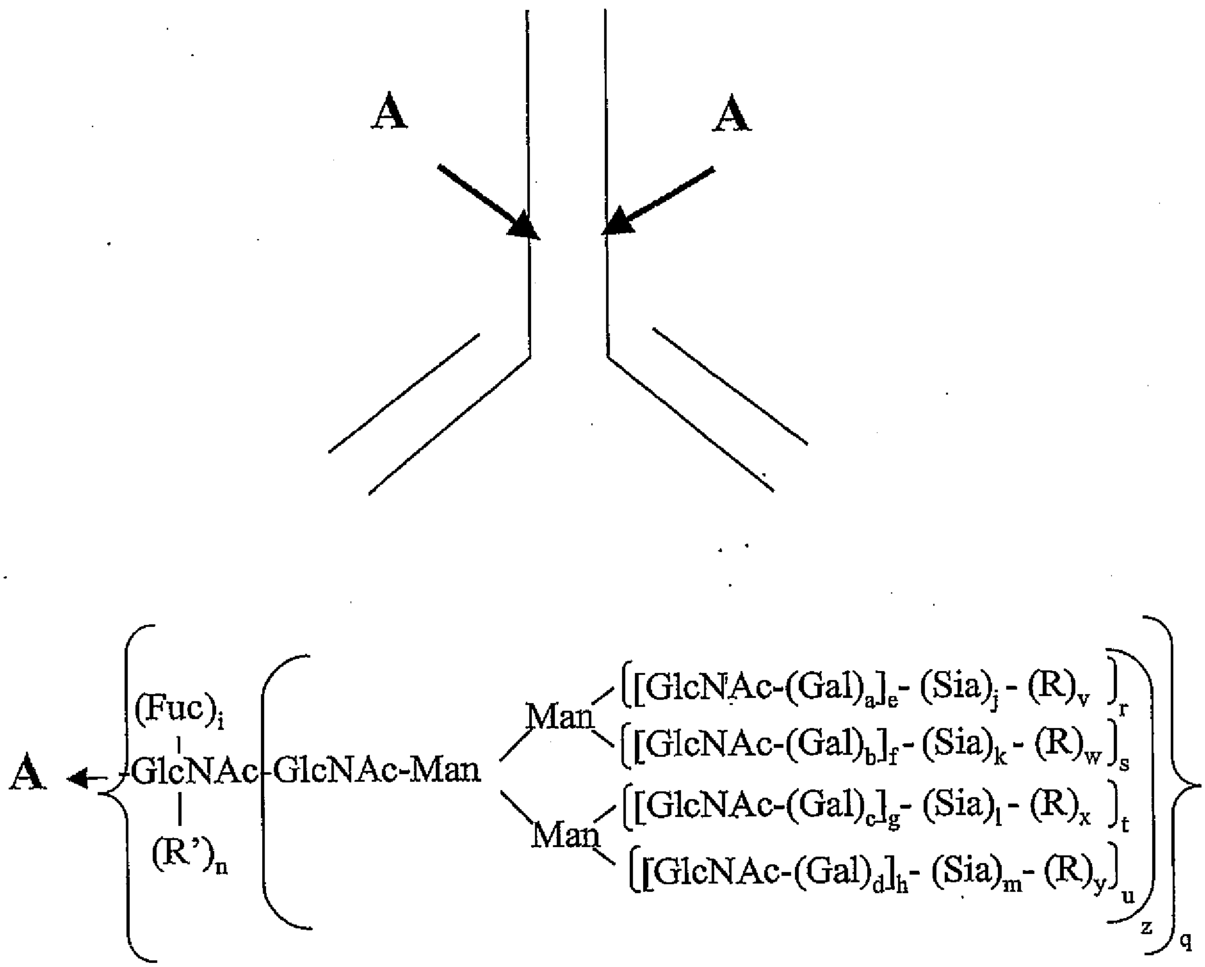

E. coli expressed Reopro(N)—no mucin peptide.
a-e, n = 0.
1. NHS-CO-linker-SA-CMP
2. ST3Gal3, asialo-transferrin
3. CMP-SA, ST3Gal3
a-e = 0; n = 1; R' = linker-transferrin.

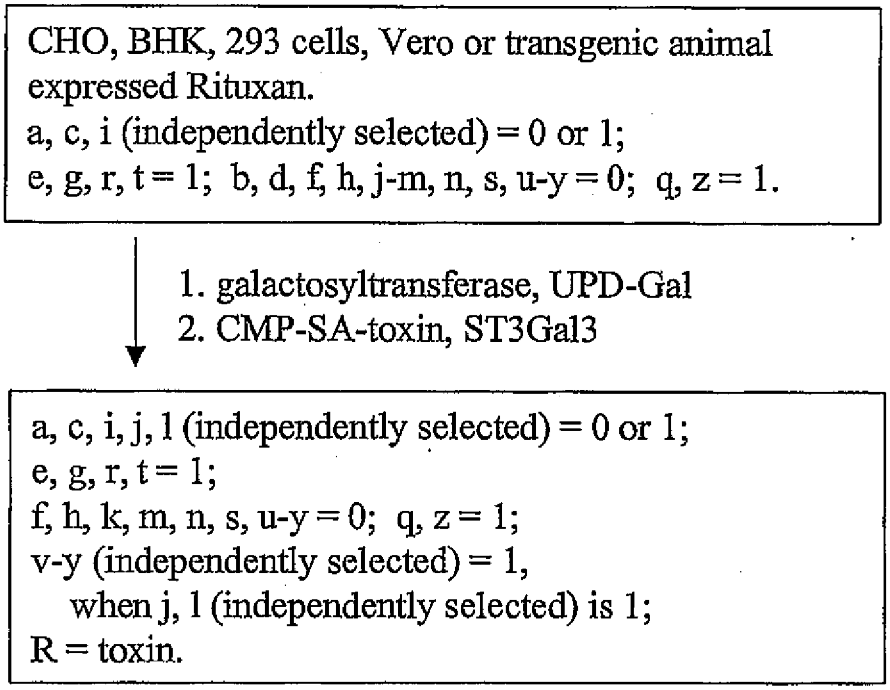
FIG. 50L


A
A
A
(Fuc)$_i$
GlcNAc
(R')$_n$
GlcNAc-Man
Man
Man
[[GlcNAc-(Gal)$_a$]$_e$- (Sia)$_j$ - (R)$_v$]$_r$
[[GlcNAc-(Gal)$_b$]$_f$ - (Sia)$_k$ - (R)$_w$]$_s$
[[GlcNAc-(Gal)$_c$]$_g$- (Sia)$_l$ - (R)$_x$]$_t$
[[GlcNAc-(Gal)$_d$]$_h$- (Sia)$_m$- (R)$_y$]$_u$
z
q

a-d, i, q-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
j-m (independently selected) = 0 or 1.
n, v-y = 0; z = 0 or 1; R = polymer, toxin, radioisotope-complex, drug, glycoconjugate.
R' = H, sugar, glycoconjugate.

z

FIG. 51A

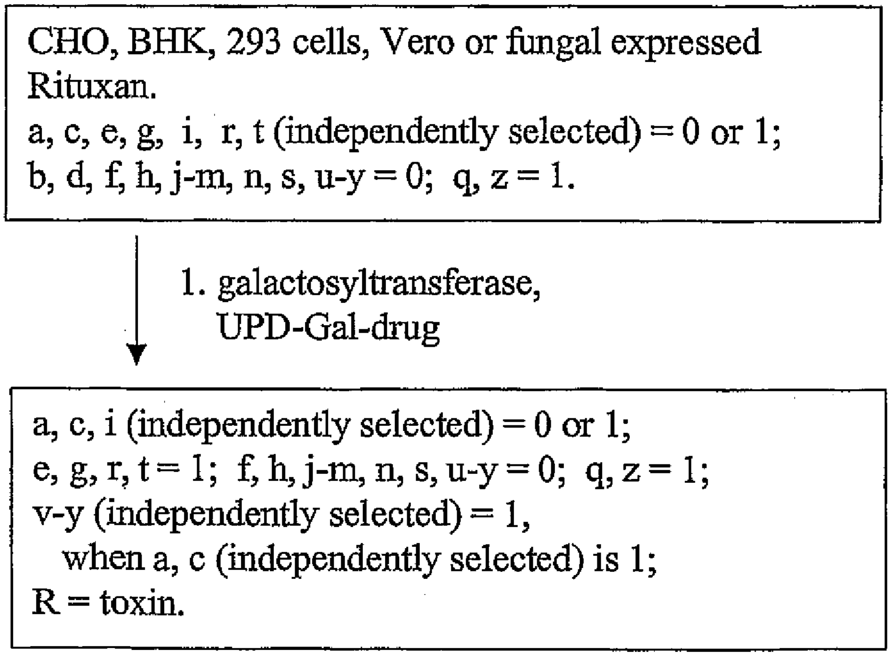


CHO, BHK, 293 cells, Vero or transgenic animal expressed Rituxan.
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0; q, z = 1.

1. galactosyltransferase, UPD-Gal
2. CMP-SA-toxin, ST3Gal3

a, c, i, j, l (independently selected) = 0 or 1;
e, g, r, t = 1;
f, h, k, m, n, s, u-y = 0; q, z = 1;
v-y (independently selected) = 1,
when j, l (independently selected) is 1;
R = toxin.

FIG. 51B

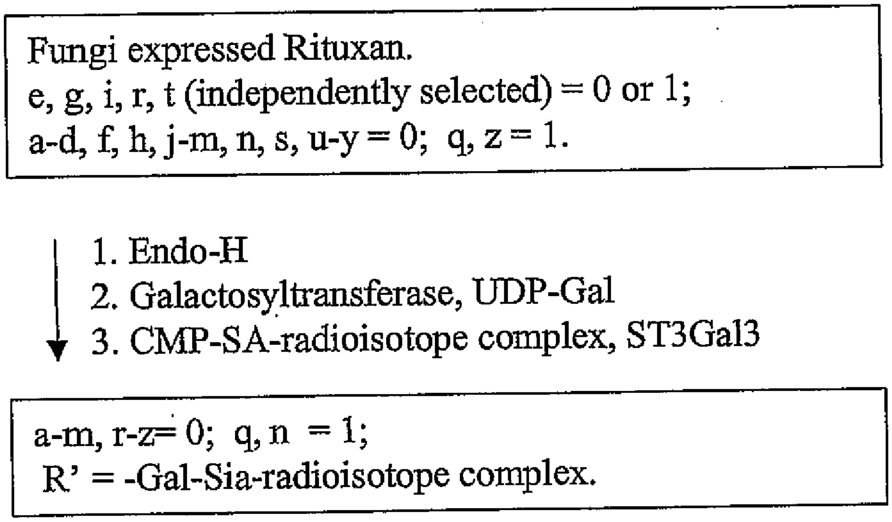


CHO, BHK, 293 cells, Vero or fungal expressed Rituxan.
a, c, e, g, i, r, t (independently selected) = 0 or 1;
b, d, f, h, j-m, n, s, u-y = 0; q, z = 1.

1. galactosyltransferase, UPD-Gal-drug

a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, j-m, n, s, u-y = 0; q, z = 1;
v-y (independently selected) = 1,
when a, c (independently selected) is 1;
R = toxin.

FIG. 51C

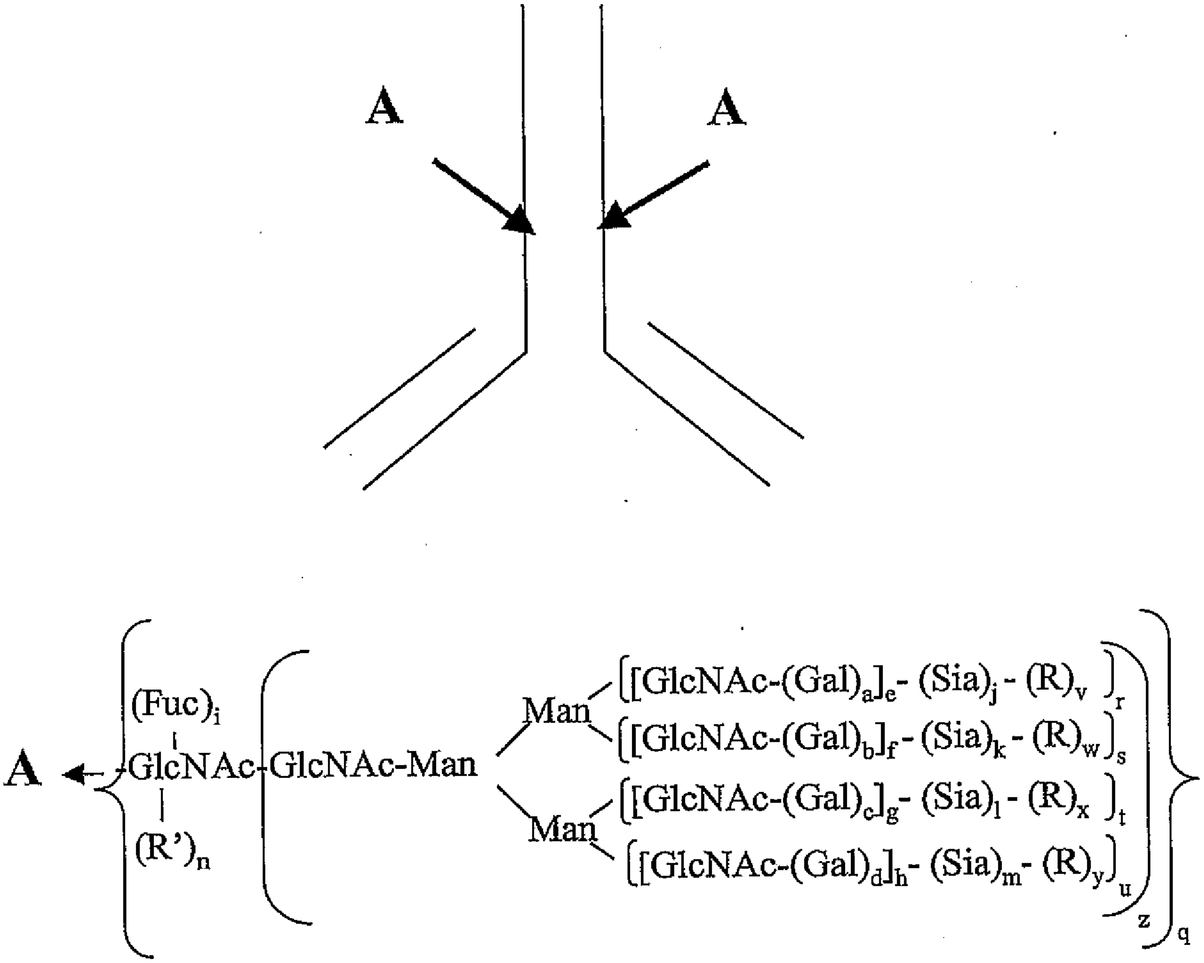


Fungi expressed Rituxan.
e, g, i, r, t (independently selected) = 0 or 1;
a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.

1. Endo-H
2. Galactosyltransferase, UDP-Gal
3. CMP-SA-radioisotope complex, ST3Gal3

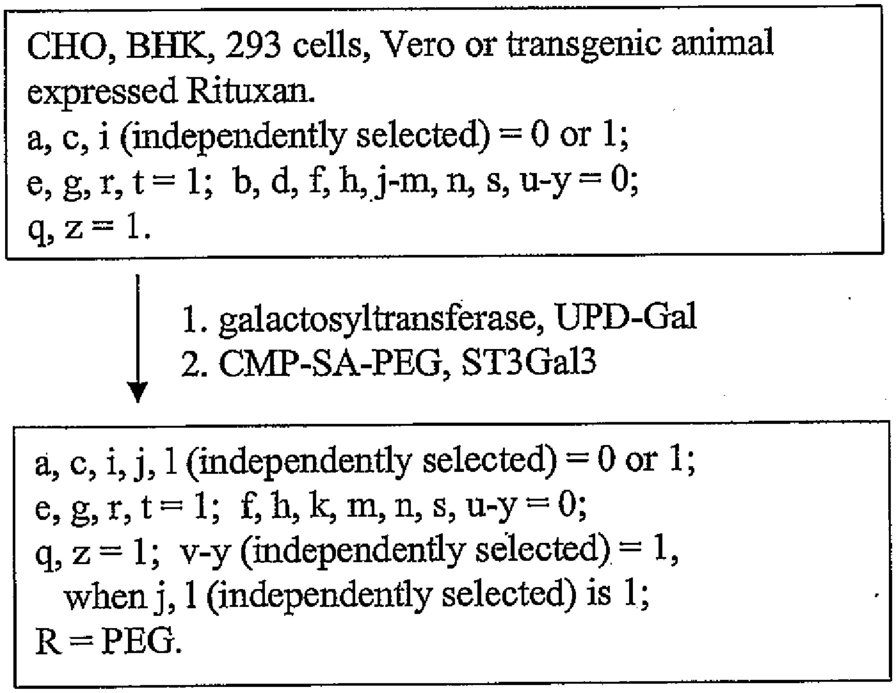
a-m, r-z= 0; q, n = 1;
R' = -Gal-Sia-radioisotope complex.

FIG. 51D


A
A
A
(Fuc)$_i$
GlcNAc-GlcNAc-Man
(R')$_n$
Man
Man
[[GlcNAc-(Gal)$_a$]$_e$- (Sia)$_j$ - (R)$_v$]$_r$
[[GlcNAc-(Gal)$_b$]$_f$ - (Sia)$_k$ - (R)$_w$]$_s$
[[GlcNAc-(Gal)$_c$]$_g$- (Sia)$_l$ - (R)$_x$]$_t$
[[GlcNAc-(Gal)$_d$]$_h$- (Sia)$_m$- (R)$_y$]$_u$
z
q

a-d, i, q-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
j-m (independently selected) = 0 or 1.
n, v-y = 0; z = 0 or 1;
R = polymer, toxin, radioisotope-complex, drug, glycoconjugate, mannose, oligo-mannose.
R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 51E

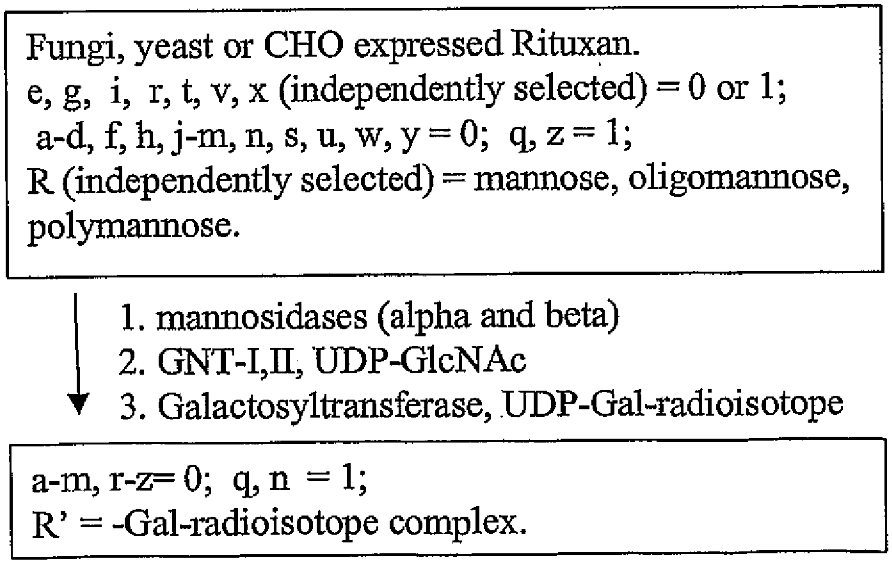


CHO, BHK, 293 cells, Vero or transgenic animal expressed Rituxan.
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;
q, z = 1.

1. galactosyltransferase, UPD-Gal
2. CMP-SA-PEG, ST3Gal3

a, c, i, j, l (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, k, m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1, when j, l (independently selected) is 1;
R = PEG.

FIG. 51F



Fungi, yeast or CHO expressed Rituxan.
e, g, i, r, t, v, x (independently selected) = 0 or 1;
a-d, f, h, j-m, n, s, u, w, y = 0; q, z = 1;
R (independently selected) = mannose, oligomannose, polymannose.

1. mannosidases (alpha and beta)
2. GNT-I,II, UDP-GlcNAc
3. Galactosyltransferase, UDP-Gal-radioisotope

a-m, r-z= 0; q, n = 1;
R' = -Gal-radioisotope complex.

FIG. 51G

FIG. 52A

ACCCCCCTGGGCCCTGCCAGCTCCCTGCCCCAGAGCTTCCTGCTCAAT
GCTTAGAGCAAGTGAGGAAGATCCAGGGCGATGGCGCAGCGCTCCAG
GAGAAGCTGTGTGCCACCTACAAGCTGTGCCACCCCGAGGAGCTGGT
GCTGCTCGGACACTCTCTGGGCATCCCCTGGGCTCCCCTGAGCAGCTG
CCCCAGCCAGGCCCTGCAGCTGGCAGGCTGCTTGAGCCAACTCCATA
GCGGCCTTTTCCTCTACCAGGGGCTCCTGCAGGCCCTGGAAGGGATCT
CCCCCGAGTTGGGTCCCACCTTGGACACACTGCAGCTGGACGTCGCCG
ACTTTGCCACCACCATCTGGCAGCAGATGGAAGAACTGGGAATGGCC
CCTGCCCTGCAGCCCACCCAGGGTGCCATGCCGGCCTTCGCCTCTGCT
TTCCAGCGCCGGGCAGGAGGGGTCCTGGTTGCCTCCCATCTGCAGAG
CTTCCTGGAGGTGTCGTACCGCGTTCTACGCCACCTTGCCCAGCCCTG
A

FIG. 52B

Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu Glu
Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr
Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro
Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser
Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe
Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro
Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val
Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His
Leu Ala Gln Pro

FIG. 53B

Met Ala Leu Thr Phe Ala Leu Leu Val Ala Leu Leu Val Leu Ser Cys Lys Ser
Ser Cys Ser Val Gly Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr
Leu Met Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln Lys Ala
Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe Asn Leu Phe Ser Thr
Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu Leu Asp Lys Phe Tyr Thr Glu
Leu Tyr Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Ile Gln Gly Val Gly Val
Thr Glu Thr Pro Leu Met Lys Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe
Gln Arg Ile Thr Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val
Val Arg Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser Leu
Arg Ser Lys Glu

FIG. 54A

ATGACCAACAAGTGTCTCCTCCAAATTGCTCTCCTGTTGTGCTTCTCC
ACTACAGCTCTTTCCATGAGCTACAACTTGCTTGGATTCCTACAAAGA
AGCAGCAATTTTCAGTGTCAGAAGCTCCTGTGGCAATTGAATGGGAG
GCTTGAATATTGCCTCAAGGACAGGATGAACTTTGACATCCCTGAGG
AGATTAAGCAGCTGCAGCAGTTCCAGAAGGAGGACGCCGCATTGACC
ATCTATGAGATGCTCCAGAACATCTTTGCTATTTTCAGACAAGATTCA
TCTAGCACTGGCTGGAATGAGACTATTGTTGAGAACCTCCTGGCTAA
TGTCTATCATCAGATAAACCATCTGAAGACAGTCCTGGAAGAAAAAC
TGGAGAAAGAAGATTTTACCAGGGGAAAACTCATGAGCAGTCTGCAC
CTGAAAAGATATTATGGGAGGATTCTGCATTACCTGAAGGCCAAGGA
GTACAGTCACTGTGCCTGGACCATAGTCAGAGTGGAAATCCTAAGGA
ACTTTTACTTCATTAACAGACTTACAGGTTACCTCCGAAACTGAAGAT
CTCCTAGCCTGTCCCTCTGGGACTGGACAATTGCTTCAAGCATTCTTC
AACCAGCAGATGCTGTTTAAGTGACTGATGGCTAATGTACTGCAAAT
GAAAGGACACTAGAAGATTTTGAAATTTTTATTAAATTATGAGTTATT
TTTATTTAT TTAAATTTTATTTTGGAAAATAAATTATTTTTGGTGC

FIG. 54B

Met Thr Asn Lys Cys Leu Leu Gln Ile Ala Leu Leu Leu Cys Phe Ser Thr Thr Ala
Leu Ser Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln
Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly ArgLeu Glu Tyr Cys Leu Lys Asp
Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu
Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile Phe Arg Gln
Asp Ser Ser Ser Thr Gly Trp Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val
Tyr His Gln Ile Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp
Phe Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg Ile
Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr Ile Val Arg Val
Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg Asn

FIG. 55A

ATGGTCTCCCAGGCCCTCAGGCTCCTCTGCCTTCTGCTTGGGCTTCAG
GGCTGCCTGGCTGCAGTCTTCGTAACCCAGGAGGAAGCCCACGGCGT
CCTGCACCGGCGCCGGCGCGCCAACGCGTTCCTGGAGGAGCTGCGGC
CGGGCTCCCTGGAGAGGGAGTGCAAGGAGGAGCAGTGCTCCTTCGA
GGAGGCCCGGGAGATCTTCAAGGACGCGGAGAGGACGAAGCTGTTC
TGGATTTCTTACAGTGATGGGGACCAGTGTGCCTCAAGTCCATGCCA
GAATGGGGGCTCCTGCAAGGACCAGCTCCAGTCCTATATCTGCTTCT
GCCTCCCTGCCTTCGAGGGCCGGAACTGTGAGACGCACAAGGATGAC
CAGCTGATCTGTGTGAACGAGAACGGCGGCTGTGAGCAGTACTGCAG
TGACCACACGGGCACCAAGCGCTCCTGTCGGTGCCACGAGGGGTACT
CTCTGCTGGCAGACGGGGTGTCCTGCACACCCACAGTTGAATATCCA
TGTGGAAAAATACCTATTCTAGAAAAAAGAAATGCCAGCAAACCCCA
AGGCCGAATTGTGGGGGGCAAGGTGTGCCCCAAAGGGGAGTGTCCA
TGGCAGGTCCTGTTGTTGGTGAATGGAGCTCAGTTGTGTGGGGGGAC
CCTGATCAACACCATCTGGGTGGTCTCCGCGGCCCACTGTTTCGACAA
AATCAAGAACTGGAGGAACCTGATCGCGGTGCTGGGCGAGCACGAC
CTCAGCGAGCACGACGGGGATGAGCAGAGCCGGCGGGTGGCGCAGG
TCATCATCCCCAGCACGTACGTCCCGGGCACCACCAACCACGACATC
GCGCTGCTCCGCCTGCACCAGCCCGTGGTCCTCACTGACCATGTGGTG
CCCCTCTGCCTGCCCGAACGGACGTTCTCTGAGAGGACGCTGGCCTTC
GTGCGCTTCTCATTGGTCAGCGGCTGGGGCCAGCTGCTGGACCGTGG
CGCCACGGCCCTGGAGCTCATGGTGCTCAACGTGCCCCGGCTGATGA
CCCAGGACTGCCTGCAGCAGTCACGGAAGGTGGGAGACTCCCCAAAT
ATCACGGAGTACATGTTCTGTGCCGGCTACTCGGATGGCAGCAAGGA
CTCCTGCAAGGGGGACAGTGGAGGCCCACATGCCACCCACTACCGGG
GCACGTGGTACCTGACGGGCATCGTCAGCTGGGGCCAGGGCTGCGCA
ACCGTGGGCCACTTTGGGGTGTACACCAGGGTCTCCCAGTACATCGA
GTGGCTGCAAAAGCTCATGCGCTCAGAGCCACGCCCAGGAGTCCTCC
TGCGAGCCCCATTTCCC

FIG. 55B

Met Val Ser Gln Ala Leu Arg Leu Leu Cys Leu Leu Leu Gly Leu Gln Gly Cys
Leu Ala Ala Val Phe Val Thr Gln Glu Glu Ala His Gly Val Leu His Arg Arg Arg
Arg Ala Asn Ala Phe Leu Glu Glu Leu Arg Pro Gly Ser Leu Glu Arg Glu Cys
Lys Glu Glu Gln Cys Ser Phe Glu Glu Ala Arg Glu Ile Phe Lys Asp Ala Glu Arg
Thr Lys Leu Phe Trp Ile Ser Tyr Ser Asp Gly Asp Gln Cys Ala Ser Ser Pro Cys
Gln Asn Gly Gly Ser Cys Lys Asp Gln Leu Gln Ser Tyr Ile Cys Phe Cys Leu Pro
Ala Phe Glu Gly Arg Asn Cys Glu Thr His Lys Asp Asp Gln Leu Ile Cys Val
Asn Glu Asn Gly Gly Cys Glu Gln Tyr Cys Ser Asp His Thr Gly Thr Lys Arg
Ser Cys Arg Cys His Glu Gly Tyr Ser Leu Leu Ala Asp Gly Val Ser Cys Thr Pro
Thr Val Glu Tyr Pro Cys Gly Lys Ile Pro Ile Leu Glu Lys Arg Asn Ala Ser Lys
Pro Gln Gly Arg Ile Val Gly Gly Lys Val Cys Pro Lys Gly Glu Cys Pro Trp Gln
Val Leu Leu Leu Val Asn Gly Ala Gln Leu Cys Gly Gly Thr Leu Ile Asn Thr Ile
Trp Val Val Ser Ala Ala His Cys Phe Asp Lys Ile Lys Asn Trp Arg Asn Leu Ile
Ala Val Leu Gly Glu His Asp Leu Ser Glu His Asp Gly Asp Glu Gln Ser Arg
Arg Val Ala Gln Val Ile Ile Pro Ser Thr Tyr Val Pro Gly Thr Thr Asn His Asp
Ile Ala Leu Leu Arg Leu His Gln Pro Val Val Leu Thr Asp His Val Val Pro Leu
Cys Leu Pro Glu Arg Thr Phe Ser Glu Arg Thr Leu Ala Phe Val Arg Phe Ser
Leu Val Ser Gly Trp Gly Gln Leu Leu Asp Arg Gly Ala Thr Ala Leu Glu Leu
Met Val Leu Asn Val Pro Arg Leu Met Thr Gln Asp Cys Leu Gln Gln Ser Arg
Lys Val Gly Asp Ser Pro Asn Ile Thr Glu Tyr Met Phe Cys Ala Gly Tyr Ser Asp
Gly Ser Lys Asp Ser Cys Lys Gly Asp Ser Gly Gly Pro His Ala Thr His Tyr Arg
Gly Thr Trp Tyr Leu Thr Gly Ile Val Ser Trp Gly Gln Gly Cys Ala Thr Val Gly
His Phe Gly Val Tyr Thr Arg Val Ser Gln Tyr Ile Glu Trp Leu Gln Lys Leu Met
Arg Ser Glu Pro Arg Pro Gly Val Leu Leu Arg Ala Pro Phe Pro

FIG. 56A

ATGCAGCGCGTGAACATGATCATGGCAGAATCACCAAGCCTCATCAC
CATCTGCCTTTTAGGATATCTACTCAGTGCTGAATGTACAGTTTTTCTT
GATCATGAAAACGCCAACAAAATTCTGAATCGGCCAAAGAGGTATAA
TTCAGGTAAATTGGAAGAGTTTGTTCAAGGGAACCTTGAGAGAGAAT
GTATGGAAGAAAAGTGTAGTTTTGAAGAACCACGAGAAGTTTTTGAA
AACACTGAAAAGACAACTGAATTTTGGAAGCAGTATGTTGATGGAGA
TCAGTGTGAGTCCAATCCATGTTTAAATGGCGGCAGTTGCAAGGATG
ACATTAATTCCTATGAATGTTGGTGTCCCTTTGGATTTGAAGGAAAGA
ACTGTGAATTAGATGTAACATGTAACATTAAGAATGGCAGATGCGAG
CAGTTTTGTAAAAATAGTGCTGATAACAAGGTGGTTTGCTCCTGTACT
GAGGGATATCGACTTGCAGAAAACCAGAAGTCCTGTGAACCAGCAGT
GCCATTTCCATGTGGAAGAGTTTCTGTTTCACAAACTTCTAAGCTCAC
CCGTGCTGAGGCTGTTTTTCCTGATGTGGACTATGTAAATCCTACTGA
AGCTGAAACCATTTTGGATAACATCACTCAAGGCACCCAATCATTTA
ATGACTTCACTCGGGTTGTTGGTGGAGAAGATGCCAAACCAGGTCAA
TTCCCTTGGCAGGTTGTTTTGAATGGTAAAGTTGATGCATTCTGTGGA
GGCTCTATCGTTAATGAAAAATGGATTGTAACTGCTGCCCACTGTGTT
GAAACTGGTGTTAAAATTACAGTTGTCGCAGGTGAACATAATATTGA
GGAGACAGAACATACAGAGCAAAAGCGAAATGTGATTCGAGCAATT
ATTCCTCACCACAACTACAATGCAGCTATTAATAAGTACAACCATGA
CATTGCCCTTCTGGAACTGGACGAACCCTTAGTGCTAAACAGCTACG
TTACACCTATTTGCATTGCTGACAAGGAATACACGAACATCTTCCTCA
AATTTGGATCTGGCTATGTAAGTGGCTGGGCAAGAGTCTTCCACAAA
GGGAGATCAGCTTTAGTTCTTCAGTACCTTAGAGTTCCACTTGTTGAC
CGAGCCACATGTCTTCGATCTACAAAGTTCACCATCTATAACAACAT
GTTCTGTGCTGGCTTCCATGAAGGAGGTAGAGATTCATGTCAAGGAG
ATAGTGGGGGACCCCATGTTACTGAAGTGGAAGGGACCAGTTTCTTA
ACTGGAATTATTAGCTGGGGTGAAGAGTGTGCAATGAAAGGCAAATA
TGGAATATATACCAAGGTATCCCGGTATGTCAACTGGATTAAGGAAA
AAACAAAGCTCACTTAATGAAAGATGGATTTCCAAGGTTAATTCATT
GGAATTGAAAATTAACAG

FIG. 56B

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Ser Leu Ile Thr Ile Cys Leu
Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe LeuAsp His Glu Asn Ala
Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn Ser Gly Lys Leu Glu Glu Phe
Val Gln Gly Asn Leu Glu Arg Glu Cys Met Glu Glu Lys Cys Ser Phe Glu Glu
Pro Arg Glu Val Phe Glu Asn Thr Glu Lys Thr Thr Glu Phe Trp Lys Gln Tyr
Val Asp Gly Asp Gln Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys
Asp Asp Ile Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn
Cys Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe Cys
Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly Tyr Arg Leu
Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser
Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Ala Val Phe Pro Asp Val Asp Tyr
Val Asn Pro Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile Thr Gln Gly Thr Gln Ser
Phe Asn Asp Phe Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe
Pro Trp Gln Val Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val
Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr
Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn
Val Ile Arg Ala Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn
His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr
Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly
Tyr Val Ser Gly Trp Ala Arg Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln
Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Arg Ser Thr Lys Phe
Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu
Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr
Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr

FIG. 57A

ATGGATTACTACAGAAAATATGCAGCTATCTTTCTGGTCACATTGTCG
GTGTTTCTGCATGTTCTCCATTCCGCTCCTGATGTGCAGGATTGCCCA
GAATGCACGCTACAGGAAAACCCATTCTTCTCCCAGCCGGGTGCCCC
AATACTTCAGTGCATGGGCTGCTGCTTCTCTAGAGCATATCCCACTCC
ACTAAGGTCCAAGAAGACGATGTTGGTCCAAAAGAACGTCACCTCAG
AGTCCACTTGCTGTGTAGCTAAATCATATAACAGGGTCACAGTAATG
GGGGGTTTCAAAGTGGAGAACCACACGGCGTGCCACTGCAGTACTTG
TTATTATCACAAATCTTAAATGTTTTACCAAGTGCTGTCTTGATGACT
GCTGATTTTCTGGAATGGAAAATTAAGTTGTTTAGTGTTTATGGCTTT
GTGAGATAAAACTCTCCTTTTCCTTACCATACCACTTTGACACGCTTC
AAGGATATACTGCAGCTTTACTGCCTTCCTCCTTATCCTACAGTACAA
TCAGCAGTCTAGTTCTTTTCATTTGGAATGAATACAGCATTAAGCTTG
TTCCACTGCAAATAAAGCCTTTTAAATCATC

FIG. 57B

Met Asp Tyr Tyr Arg Lys Tyr Ala Ala Ile Phe Leu Val Thr Leu Ser Val Phe Leu
His Val Leu His Ser Ala Pro Asp Val Gln Asp Cys Pro Glu Cys Thr Leu Gln Glu
Asn Pro Phe Phe Ser Gln Pro Gly Ala Pro Ile Leu Gln Cys Met Gly Cys Cys Phe
Ser Arg Ala Tyr Pro Thr Pro Leu Arg Ser Lys Lys Thr Met Leu Val Gln Lys Asn
Val Thr Ser Glu Ser Thr Cys Cys Val Ala Lys Ser Tyr Asn Arg Val Thr Val Met
Gly Gly Phe Lys Val Glu Asn His Thr Ala Cys His Cys Ser Thr Cys Tyr Tyr His
Lys Ser

FIG. 57C

ATGAAGACACTCCAGTTTTTCTTCCTTTTCTGTTGCTGGAAAGCAATC
TGCTGCAATAGCTGTGAGCTGACCAACATCACCATTGCAATAGAGAA
AGAAGAATGTCGTTTCTGCATAAGCATCAACACCACTTGGTGTGCTG
GCTACTGCTACACCAGGGATCTGGTGTATAAGGACCCAGCCAGGCCC
AAAATCCAGAAAACATGTACCTTCAAGGAACTGGTATATGAAACAGT
GAGAGTGCCCGGCTGTGCTCACCATGCAGATTCCTTGTATACATACCC
AGTGGCCACCCAGTGTCACTGTGGCAAGTGTGACAGCGACAGCACTG
ATTGTACTGTGCGAGGCCTGGGGCCCAGCTACTGCTCCTTTGGTGAAA
TGAAAGAATAA

FIG. 57D

Met Lys Thr Leu Gln Phe Phe Phe Leu Phe Cys Cys Trp Lys Ala Ile Cys Cys
Asn Ser Cys Glu Leu Thr Asn Ile Thr Ile Ala Ile Glu Lys Glu Glu Cys Arg Phe
Cys Ile Ser Ile Asn Thr Thr Trp Cys Ala Gly Tyr Cys Tyr Thr Arg Asp Leu Val
Tyr Lys Asp Pro Ala Arg Pro Lys Ile Gln Lys Thr Cys Thr Phe Lys Glu Leu Val
Tyr Glu Thr Val Arg Val Pro Gly Cys Ala His His Ala Asp Ser Leu Tyr Thr Tyr
Pro Val Ala Thr Gln Cys His Cys Gly Lys Cys Asp Ser Asp Ser Thr Asp Cys
Thr Val Arg Gly Leu Gly Pro Ser Tyr Cys Ser Phe Gly Glu Met Lys Glu

FIG. 58A

CCCGGAGCCGGACCGGGGCCACCGCGCCCGCTCTGCTCCGACACCGC
GCCCCCTGGACAGCCGCCCTCTCCTCCAGGCCCGTGGGGCTGGCCCT
GCACCGCCGAGCTTCCCGGGATGAGGGCCCCCGGTGTGGTCACCCGG
CGCGCCCCAGGTCGCTGAGGGACCCCGGCCAGGCGCGGAGATGGGG
GTGCACGAATGTCCTGCCTGGCTGTGGCTTCTCCTGTCCCTGCTGTCG
CTCCCTCTGGGCCTCCCAGTCCTGGGCGCCCCACCACGCCTCATCTGT
GACAGCCGAGTCCTGGAGAGGTACCTCTTGGAGGCCAAGGAGGCCG
AGAATATCACGACGGGCTGTGCTGAACACTGCAGCTTGAATGAGAAT
ATCACTGTCCCAGACACCAAAGTTAATTTCTATGCCTGGAAGAGGAT
GGAGGTCGGGCAGCAGGCCGTAGAAGTCTGGCAGGGCCTGGCCCTG
CTGTCGGAAGCTGTCCTGCGGGGCCAGGCCCTGTTGGTCAACTCTTCC
CAGCCGTGGGAGCCCCTGCAGCTGCATGTGGATAAAGCCGTCAGTGG
CCTTCGCAGCCTCACCACTCTGCTTCGGGCTCTGCGAGCCCAGAAGG
AAGCCATCTCCCCTCCAGATGCGGCCTCAGCTGCTCCACTCCGAACA
ATCACTGCTGACACTTTCCGCAAACTCTTCCGAGTCTACTCCAATTTC
CTCCGGGGAAAGCTGAAGCTGTACACAGGGGAGGCCTGCAGGACAG
GGGACAGATGACCAGGTGTGTCCACCTGGGCATATCCACCACCTCCC
TCACCAACATTGCTTGTGCCACACCCTCCCCCGCCACTCCTGAACCCC
GTCGAGGGGCTCTCAGCTCAGCGCCAGCCTGTCCCATGGACACTCCA
GTGCCAGCAATGACATCTCAGGGGCCAGAGGAACTGTCCAGAGAGC
AACTCTGAGATCTAAGGATGTCACAGGGCCAACTTGAGGGCCCAGAG
CAGGAAGCATTCAGAGAGCAGCTTTAAACTCAGGGACAGAGCCATG
CTGGGAAGACGCCTGAGCTCACTCGGCACCCTGCAAAATTTGATGCC
AGGACACGCTTTGGAGGCGATTTACCTGTTTTCGCACCTACCATCAGG
GACAGGATGACCTGGAGAACTTAGGTGGCAAGCTGTGACTTCTCCAG
GTCTCACGGGCATGGGCACTCCCTTGGTGGCAAGAGCCCCCTTGACA
CCGGGGTGGTGGGAACCATGAAGACAGGATGGGGGCTGGCCTCTGG
CTCTCATGGGGTCCAAGTTTTGTGTATTCTTCAACCTCATTGACAAGA
ACTGAAACCACCAAAAAAAAAAAAAA

FIG. 58B

Met Gly Val His Glu Cys Pro Ala Trp Leu Trp Leu Leu Leu Ser Leu Leu Ser
Leu Pro Leu Gly Leu Pro Val Leu Gly Ala Pro Pro Arg Leu Ile Cys Asp Ser
Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr
Gly Cys Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val Glu Val
Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly Gln Ala Leu Leu
Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp Lys Ala Val Ser
Gly Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu Arg Ala Gln Lys Glu Ala Ile
Ser Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe
Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr
Thr Gly Glu Ala Cys Arg Thr Gly Asp Arg

FIG. 59A

ATGTGGCTGCAGAGCCTGCTGCTCTTGGGCACTGTGGCCTGCAGCAT
CTCTGCACCCGCCCGCTCGCCCAGCCCCAGCACGCAGCCCTGGGAGC
ATGTGAATGCCATCCAGGAGGCCCGGCGTCTCCTGAACCTGAGTAGA
GACACTGCTGCTGAGATGAATGAAACAGTAGAAGTCATCTCAGAAAT
GTTTGACCTCCAGGAGCCGACCTGCCTACAGACCCGCCTGGAGCTGT
ACAAGCAGGGCCTGCGGGGCAGCCTCACCAAGCTCAAGGGCCCCTTG
ACCATGATGGCCAGCCACTACAAGCAGCACTGCCCTCCAACCCCGGA
AACTTCCTGTGCAACCCAGATTATCACCTTTGAAAGTTTCAAAGAGA
ACCTGAAGGACTTTCTGCTTGTCATCCCCTTTGACTGCTGGGAGCCAG
TCCAGGAGTGA

FIG. 59B

Met Trp Leu Gln Ser Leu Leu Leu Leu Gly Thr Val Ala Cys Ser Ile Ser Ala Pro
Ala Arg Ser Pro Ser Pro Ser Thr Gln Pro Trp Glu His Val Asn Ala Ile Gln Glu
Ala Arg Arg Leu Leu Asn Leu Ser Arg Asp Thr Ala Ala Glu Met Asn Glu Thr
Val Glu Val Ile Ser Glu Met Phe Asp Leu Gln Glu Pro Thr Cys Leu Gln Thr Arg
Leu Glu Leu Tyr Lys Gln Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro
Leu Thr Met Met Ala Ser His Tyr Lys Gln His Cys Pro Pro Thr Pro Glu Thr Ser
Cys Ala Thr Gln Ile Ile Thr Phe Glu Ser Phe Lys Glu Asn Leu Lys Asp Phe Leu
Leu Val Ile Pro Phe Asp Cys Trp Glu Pro Val Gln Glu

FIG. 60A

ATGAAATATACAAGTTATATCTTGGCTTTTCAGCTCTGCATCGTTTTG
GGTTCTCTTGGCTGTTACTGCCAGGACCCATATGTAAAAGAAGCAGA
AAACCTTAAGAAATATTTTAATGCAGGTCATTCAGATGTAGCGGATA
ATGGAACTCTTTTCTTAGGCATTTTGAAGAATTGGAAAGAGGAGAGT
GACAGAAAAATAATGCAGAGCCAAATTGTCTCCTTTTACTTCAAACT
TTTTAAAAACTTTAAAGATGACCAGAGCATCCAAAAGAGTGTGGAGA
CCATCAAGGAAGACATGAATGTCAAGTTTTTCAATAGCAACAAAAAG
AAACGAGATGACTTCGAAAAGCTGACTAATTATTCGGTAACTGACTT
GAATGTCCAACGCAAAGCAATACATGAACTCATCCAAGTGATGGCTG
AACTGTCGCCAGCAGCTAAAACAGGGAAGCGAAAAAGGAGTCAGAT
GCTGTTTCGAGGTCGAAGAGCATCCCAGTAA

FIG. 60B

Met Lys Tyr Thr Ser Tyr Ile Leu Ala Phe Gln Leu Cys Ile Val Leu Gly Ser Leu
Gly Cys Tyr Cys Gln Asp Pro Tyr Val Lys Glu Ala Glu Asn Leu Lys Lys Tyr
Phe Asn Ala Gly His Ser Asp Val Ala Asp Asn Gly Thr Leu Phe Leu Gly Ile
Leu Lys Asn Trp Lys Glu Glu Ser Asp Arg Lys Ile Met Gln Ser Gln Ile Val Ser
Phe Tyr Phe Lys Leu Phe Lys Asn Phe Lys Asp Asp Gln Ser Ile Gln Lys Ser Val
Glu Thr Ile Lys Glu Asp Met Asn Val Lys Phe Phe Asn Ser Asn Lys Lys Lys
Arg Asp Asp Phe Glu Lys Leu Thr Asn Tyr Ser Val Thr Asp Leu Asn Val Gln
Arg Lys Ala Ile His Glu Leu Ile Gln Val Met Ala Glu Leu Ser Pro Ala Ala Lys
Thr Gly Lys Arg Lys Arg Ser Gln Met Leu Phe Arg Gly Arg Arg Ala Ser Gln

FIG. 61A

CTGGGACAGTGAATCGACAATGCCGTCTTCTGTCTCGTGGGCATCCT
CCTGCTGGCAGGCCTGTGCTGCCTGGTCCCTGTCTCCCTGGCTGAGGA
TCCCCAGGGAGATGCTGCCCAGAAGACAGATACATCCCACCATGATC
AGGATCACCCAACCTTCAACAAGATCACCCCCAACCTGGCTGAGTTC
GCCTTCAGCCTATACCGCCAGCTGGCACACCAGTCCAACAGCACCAA
TATCTTCTTCTCCCCAGTGAGCATCGCTACAGCCTTTGCAATGCTCTC
CCTGGGGACCAAGGCTGACACTCACGATGAAATCCTGGAGGGCCTGA
ATTTCAACCTCACGGAGATTCCGGAGGCTCAGATCCATGAAGGCTTC
CAGGAACTCCTCCGTACCCTCAACCAGCCAGACAGCCAGCTCCAGCT
GACCACCGGCAATGGCCTGTTCCTCAGCGAGGGCCTGAAGCTAGTGG
ATAAGTTTTTGGAGGATGTTAAAAAGTTGTACCACTCAGAAGCCTTC
ACTGTCAACTTCGGGGACACCGAAGAGGCCAAGAAACAGATCAACG
ATTACGTGGAGAAGGGTACTCAAGGGAAAATTGTGGATTTGGTCAAG
GAGCTTGACAGAGACACAGTTTTTGCTCTGGTGAATTACATCTTCTTT
AAAGGCAAATGGGAGAGACCCTTTGAAGTCAAGGACACCGAGGAAG
AGGACTTCCACGTGGACCAGGTGACCACCGTGAAGGTGCCTATGATG
AAGCGTTTAGGCATGTTTAACATCCAGCACTGTAAGAAGCTGTCCAG
CTGGGTGCTGCTGATGAAATACCTGGGCAATGCCACCGCCATCTTCT
TCCTGCCTGATGAGGGGAAACTACAGCACCTGGAAAATGAACTCACC
CACGATATCATCACCAAGTTCCTGGAAAATGAAGACAGAAGGTCTGC
CAGCTTACATTTACCCAAACTGTCCATTACTGGAACCTATGATCTGAA
GAGCGTCCTGGGTCAACTGGGCATCACTAAGGTCTTCAGCAATGGGG
CTGACCTCTCCGGGGTCACAGAGGAGGCACCCCTGAAGCTCTCCAAG
GCCGTGCATAAGGCTGTGCTGACCATCGACGAGAAAGGGACTGAAGC
TGCTGGGGCCATGTTTTTAGAGGCCATACCCATGTCTATCCCCCCCGA
GGTCAAGTTCAACAAACCCTTTGTCTTCTTAATGATTGAACAAAATAC
CAAGTCTCCCCTCTTCATGGGAAAAGTGGTGAATCCCACCCAAAAAT
AACTGCCTCTCGCTCCTCAACCCCTCCCCTCCATCCCTGGCCCCCTCC
CTGGATGACATTAAAGAAGGGTTGAGCTGG

FIG. 61B

Met Pro Ser Ser Val Ser Trp Gly Ile Leu Leu Leu Ala Gly Leu Cys Cys Leu Val
Pro Val Ser Leu Ala Glu Asp Pro Gln Gly Asp Ala Ala Gln Lys Thr Asp Thr Ser
His His Asp Gln Asp His Pro Thr Phe Asn Lys Ile Thr Pro Asn Leu Ala Glu Phe
Ala Phe Ser Leu Tyr Arg Gln Leu Ala His Gln Ser Asn Ser Thr Asn Ile Phe Phe
Ser Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu Ser Leu Gly Thr Lys Ala Asp
Thr His Asp Glu Ile Leu Glu Gly Leu Asn Phe Asn Leu Thr Glu Ile Pro Glu Ala
Gln Ile His Glu Gly Phe Gln Glu Leu Leu Arg Thr Leu Asn Gln Pro Asp Ser Gln
Leu Gln Leu Thr Thr Gly Asn Gly Leu Phe Leu Ser Glu Gly Leu Lys Leu Val
Asp Lys Phe Leu Glu Asp Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr Val
Asn Phe Gly Asp Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr Val Glu Lys
Gly Thr Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu Asp Arg Asp Thr Val
Phe Ala LeuVal Asn Tyr Ile Phe Phe Lys Gly Lys Trp Glu Arg Pro Phe Glu Val
Lys Asp Thr Glu Glu Glu Asp Phe His Val Asp Gln Val Thr Thr Val Lys Val
Pro Met Met Lys Arg Leu Gly Met Phe Asn Ile Gln His Cys Lys Lys Leu Ser
Ser Trp Val Leu Leu Met Lys Tyr Leu Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro
Asp Glu Gly Lys Leu Gln His Leu Glu Asn Glu Leu Thr His Asp Ile Ile Thr Lys
Phe Leu Glu Asn Glu AspArg Arg Ser Ala Ser Leu His Leu Pro Lys Leu Ser Ile
Thr Gly Thr Tyr Asp Leu Lys Ser Val Leu Gly Gln Leu Gly Ile Thr Lys Val Phe
Ser Asn Gly Ala Asp Leu Ser Gly Val Thr Glu Glu Ala Pro Leu Lys Leu Ser Lys
Ala Val His Lys Ala Val Leu Thr Ile Asp Glu Lys Gly Thr Glu Ala Ala Gly Ala
Met Phe Leu Glu Ala Ile Pro Met Ser Ile Pro Pro Glu Val Lys Phe Asn Lys Pro
Phe Val Phe Leu Met Ile Glu Gln Asn Thr Lys Ser Pro Leu Phe Met Gly Lys Val
Val Asn Pro Thr Gln Lys

FIG. 62A-1

GCTAACCTAGTGCCTATAGCTAAGGCAGGTACCTGCATCCTTGTTTTT
GTTTAGTGGATCCTCTATCCTTCAGAGACTCTGGAACCCCTGTGGTCT
TCTCTTCATCTAATGACCCTGAGGGGATGGAGTTTTCAAGTCCTTCCA
GAGAGGAATGTCCCAAGCCTTTGAGTAGGGTAAGCATCATGGCTGGC
AGCCTCACAGGTTTGCTTCTACTTCAGGCAGTGTCGTGGGCATCAGGT
GCCCGCCCCTGCATCCCTAAAAGCTTCGGCTACAGCTCGGTGGTGTGT
GTCTGCAATGCCACATACTGTGACTCCTTTGACCCCCCGACCTTTCCT
GCCCTTGGTACCTTCAGCCGCTATGAGAGTACACGCAGTGGGCGACG
GATGGAGCTGAGTATGGGGCCCATCCAGGCTAATCACACGGGCACAG
GCCTGCTACTGACCCTGCAGCCAGAACAGAAGTTCCAGAAAGTGAAG
GGATTTGGAGGGGCCATGACAGATGCTGCTGCTCTCAACATCCTTGCC
CTGTCACCCCCTGCCCAAAATTTGCTACTTAAATCGTACTTCTCTGAA
GAAGGAATCGGATATAACATCATCCGGGTACCCATGGCCAGCTGTGA
CTTCTCCATCCGCACCTACACCTATGCAGACACCCCTGATGATTTCCA
GTTGCACAACTTCAGCCTCCCAGAGGAAGATACCAAGCTCAAGATAC
CCCTGATTCACCGAGCCCTGCAGTTGGCCCAGCGTCCCGTTTCACTCC
TTGCCAGCCCCTGGACATCACCCACTTGGCTCAAGACCAATGGAGCG
GTGAATGGGAAGGGGTCACTCAAGGGACAGCCCGGAGACATCTACC
ACCAGACCTGGGCCAGATACTTTGTGAAGTTCCTGGATGCCTATGCTG
AGCACAAGTTACAGTTCTGGGCAGTGACAGCTGAAAATGAGCCTTCT
GCTGGGCTGTTGAGTGGATACCCCTTCCAGTGCCTGGGCTTCACCCCT
GAACATCAGCGAGACTTCATTGCCCGTGACCTAGGTCCTACCCTCGCC
AACAGTACTCACCACAATGTCCGCCTACTCATGCTGGATGACCAACGC
TTGCTGCTGCCCCACTGGGCAAAGGTGGTACTGACAGACCCAGAAGC
AGCTAAATATGTTCATGGCATTGCTGTACATTGGTACCTGGACTTTCT
GGCTCCAGCCAAAGCCACCCTAGGGGAGACACACCGCCTGTTCCCCA
ACACCATGCTCTTTGCCTCAGAGGCCTGTGTGGGCTCCAAGTTCTGGG
AGCAGAGTGTGCGGCTAGGCTCCTGGGATCGAGGGATGCAGTACAGC
CACAGCATCATCACGAACCTCCTGTACCATGTGGTCGGCTGGACCGAC
TGGAACCTTGCCCTGAACCCCGAAGGAGGACCCAATTGGGTGCGTAA
CTTTGTCGACAGTCCCATCATTGTAGACATCACCAAGGACACGTTTTA
CAAACAGCCCATGTTCTACCACCTTGGCCACTTCAGCAAGTTCATTCC
TGAGGGCTCCCAGAGAGTGGGGCTGGTTGCCAGTCAGAAGAACGACC
TGGACGCAGTGGCACTGATGCATCCCGATGGCTCTGCTGTTGTGGTCG
TGCTAAACCGCTCCTCTAAGGATGTGCCTCTTACCATCAAGGATCCTG
CTGTGGGCTTCCTGGAGACAATCTCACCTGGCTACTCCATTCACACCT
ACCTGTGGCATCGCCAGTGATGGAGCAGATACTCAAGGAGGCACTGG
GCTCAGCCTGGGCATTAAAGGACAGAGTCAGCTCACACGCTGTCTG
TGACTAAAGAGGGCACAGCAGGGCCAGTGTGAGCTTACAGCGACGT

FIG. 62A-2

AAGCCCAGGGGCAATGGTTTGGGTGACTCACTTTCCCCTCTAGGTGGT
GCCCAGGGCTGGAGGCCCCTAGAAAAGATCAGTAAGCCCCAGTGTC
CCCCCAGCCCCCATGCTTATGTGAACATGCGCTGTGTGCTGCTTGCTT
TGGAAACT

FIG. 62B

Met Glu Phe Ser Ser Pro Ser Arg Glu Glu Cys Pro Lys Pro Leu Ser Arg Val Ser Ile Met Ala Gly Ser Leu Thr Gly Leu Leu Leu Leu Gln Ala Val Ser Trp Ala Ser Gly Ala Arg Pro Cys Ile Pro Lys Ser Phe Gly Tyr Ser Ser Val Val Cys Val Cys Asn Ala Thr Tyr Cys Asp Ser Phe Asp Pro Pro Thr Phe Pro Ala Leu Gly Thr Phe Ser Arg Tyr Glu Ser Thr Arg Ser Gly Arg Arg Met Glu Leu Ser Met Gly Pro Ile Gln Ala Asn His Thr Gly Thr Gly Leu Leu Leu Thr Leu Gln Pro Glu Gln Lys Phe Gln Lys Val Lys Gly Phe Gly Gly Ala Met Thr Asp Ala Ala Ala Leu Asn Ile Leu Ala Leu Ser Pro Pro Ala Gln Asn Leu Leu Leu Lys Ser Tyr Phe Ser Glu Glu Gly Ile Gly Tyr Asn Ile Ile Arg Val Pro Met Ala Ser Cys Asp Phe Ser Ile Arg Thr Tyr Thr Tyr Ala Asp Thr Pro Asp Asp Phe Gln Leu His Asn Phe Ser Leu Pro Glu Glu Asp Thr Lys Leu Lys Ile Pro Leu Ile His Arg Ala Leu Gln Leu Ala Gln Arg Pro Val Ser Leu Leu Ala Ser Pro Trp Thr Ser Pro Thr Trp Leu Lys Thr Asn Gly Ala Val Asn Gly Lys Gly Ser Leu Lys Gly Gln Pro Gly Asp Ile Tyr His Gln Thr Trp Ala Arg Tyr Phe Val Lys Phe Leu Asp Ala Tyr Ala Glu His Lys Leu Gln Phe Trp Ala Val Thr Ala Glu Asn Glu Pro Ser Ala Gly Leu Leu Ser Gly Tyr Pro Phe Gln Cys Leu Gly Phe Thr Pro Glu His Gln Arg Asp Phe Ile Ala Arg Asp Leu Gly Pro Thr Leu Ala Asn Ser Thr His His Asn Val Arg Leu Leu Met Leu Asp Asp Gln Arg Leu Leu Leu Pro His Trp Ala Lys Val Val Leu Thr Asp Pro Glu Ala Ala Lys Tyr Val His Gly Ile Ala Val His Trp Tyr Leu Asp Phe Leu Ala Pro Ala Lys Ala Thr Leu Gly Glu Thr His Arg Leu Phe Pro Asn Thr Met Leu Phe Ala Ser Glu Ala Cys Val Gly Ser Lys Phe Trp Glu Gln Ser Val Arg Leu Gly Ser Trp Asp Arg Gly Met Gln Tyr Ser His Ser Ile Ile Thr Asn Leu Leu Tyr His Val Val Gly Trp Thr Asp Trp Asn Leu Ala Leu Asn Pro Glu Gly Gly Pro Asn Trp Val Arg Asn Phe Val Asp Ser Pro Ile Ile Val Asp Ile Thr Lys Asp Thr Phe Tyr Lys Gln Pro Met Phe Tyr His Leu Gly His Phe Ser Lys Phe Ile Pro Glu Gly Ser Gln Arg Val Gly Leu Val Ala Ser Gln Lys Asn Asp Leu Asp Ala Val Ala Leu Met His Pro Asp Gly Ser Ala Val Val Val Val Leu Asn Arg Ser Ser Lys Asp Val Pro Leu Thr Ile Lys Asp Pro Ala Val Gly Phe Leu Glu Thr Ile Ser Pro Gly Tyr Ser Ile His Thr Tyr Leu Trp His Arg Gln

FIG. 63A

ATGGATGCAATGAAGAGAGGGCTCTGCTGTGTGCTGCTGCTGTGTGG
AGCAGTCTTCGTTTCGCCCAGCCAGGAAATCCATGCCCGATTCAGAA
GAGGAGCCAGATCTTACCAAGTGATCTGCAGAGATGAAAAAACGCA
GATGATATACCAGCAACATCAGTCATGGCTGCGCCCTGTGCTCAGAA
GCAACCGGGTGGAATATTGCTGGTGCAACAGTGGCAGGGCACAGTGC
CACTCAGTGCCTGTCAAAAGTTGCAGCGAGCCAAGGTGTTTCAACGG
GGGCACCTGCCAGCAGGCCCTGTACTTCTCAGATTTCGTGTGCCAGTG
CCCCGAAGGATTTGCTGGGAAGTGCTGTGAAATAGATACCAGGGCCA
CGTGCTACGAGGACCAGGGCATCAGCTACAGGGGCACGTGGAGCAC
AGCGGAGAGTGGCGCCGAGTGCACCAACTGGAACAGCAGCGCGTTG
GCCCAGAAGCCCTACAGCGGGCGGAGGCCAGACGCCATCAGGCTGG
GCCTGGGGAACCACAACTACTGCAGAAACCCAGATCGAGACTCAAA
GCCCTGGTGCTACGTCTTTAAGGCGGGGAAGTACAGCTCAGAGTTCT
GCAGCACCCCTGCCTGCTCTGAGGGAAACAGTGACTGCTACTTTGGG
AATGGGTCAGCCTACCGTGGCACGCACAGCCTCACCGAGTCGGGTGC
CTCCTGCCTCCCGTGGAATTCCATGATCCTGATAGGCAAGGTTTACAC
AGCACAGAACCCCAGTGCCCAGGCACTGGGCCTGGGCAAACATAATT
ACTGCCGGAATCCTGATGGGGATGCCAAGCCCTGGTGCCACGTGCTG
AAGAACCGCAGGCTGACGTGGGAGTACTGTGATGTGCCCTCCTGCTC
CACCTGCGGCCTGAGACAGTACAGCCAGCCTCAGTTTCGCATCAAAG
GAGGGCTCTTCGCCGACATCGCCTCCCACCCCTGGCAGGCTGCCATCT
TTGCCAAGCACAGGAGGTCGCCGGGAGAGCGGTTCCTGTGCGGGGGC
ATACTCATCAGCTCCTGCTGGATTCTCTCTGCCGCCCACTGCTTCCAG
GAGAGGTTTCCGCCCCACCACCTGACGGTGATCTTGGGCAGAACATA
CCGGGTGGTCCCTGGCGAGGAGGAGCAGAAATTTGAAGTCGAAAAA
TACATTGTCCATAAGGAATTCGATGATGACACTTACGACAATGACAT
TGCGCTGCTGCAGCTGAAATCGGATTCGTCCCGCTGTGCCCAGGAGA
GCAGCGTGGTCCGCACTGTGTGCCTTCCCCCGGCGGACCTGCAGCTG
CCGGACTGGACGGAGTGTGAGCTCTCCGGCTACGGCAAGCATGAGGC
CTTGTCTCCTTTCTATTCGGAGCGGCTGAAGGAGGCTCATGTCAGACT
GTACCCATCCAGCCGCTGCACATCACAACATTTACTTAACAGAACAG
TCACCGACAACATGCTGTGTGCTGGAGACACTCGGAGCGGCGGGCCC
CAGGCAAACTTGCACGACGCCTGCCAGGGCGATTCGGGAGGCCCCCT
GGTGTGTCTGAACGATGGCCGCATGACTTTGGTGGGCATCATCAGCT
GGGGCCTGGGCTGTGGACAGAAGGATGTCCCGGGTGTGTACACCAAG
GTTACCAACTACCTAGACTGGATTCGTGACAACATGCGACCGTGACC
AGGAACACCCGACTCCTCAAAAGCAAATGAGATCC

FIG. 63B

Met Asp Ala Met Lys Arg Gly Leu Cys Cys Val Leu Leu Leu Cys Gly Ala Val
Phe Val Ser Pro Ser Gln Glu Ile His Ala Arg Phe Arg Arg Gly Ala Arg Ser Tyr
Gln Val Ile Cys Arg Asp Glu Lys Thr Gln Met Ile Tyr Gln Gln His Gln Ser Trp
Leu Arg Pro Val Leu Arg Ser Asn Arg Val Glu Tyr Cys Trp Cys Asn Ser Gly
Arg Ala Gln Cys His Ser Val Pro Val Lys Ser Cys Ser Glu Pro Arg Cys Phe Asn
Gly Gly Thr Cys Gln Gln Ala Leu Tyr Phe Ser Asp Phe Val Cys Gln Cys Pro
Glu Gly Phe Ala Gly Lys Cys Cys Glu Ile Asp Thr Arg Ala Thr Cys Tyr Glu
Asp Gln Gly Ile Ser Tyr Arg Gly Thr Trp Ser Thr Ala Glu Ser Gly Ala Glu Cys
Thr Asn Trp Asn Ser Ser Ala Leu Ala Gln Lys Pro Tyr Ser Gly Arg Arg Pro Asp
Ala Ile Arg Leu Gly Leu Gly Asn His Asn Tyr Cys Arg Asn Pro Asp Arg Asp
Ser Lys Pro Trp Cys Tyr Val Phe Lys Ala Gly Lys Tyr Ser Ser Glu Phe Cys Ser
Thr Pro Ala Cys Ser Glu Gly Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr
Arg Gly Thr His Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn Ser Met
Ile Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala Gln Ala Leu Gly Leu
Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly Asp Ala Lys Pro Trp Cys His
Val Leu Lys Asn Arg Arg Leu Thr Trp Glu Tyr Cys Asp Val Pro Ser Cys Ser
Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro Gln Phe Arg Ile Lys Gly Gly Leu Phe
Ala Asp Ile Ala Ser His Pro Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser
Pro Gly Glu Arg Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser
Ala Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile Leu Gly
Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Glu Gln Lys Phe Glu Val Glu Lys
Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr Asp Asn Asp Ile Ala Leu
Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys Ala Gln Glu Ser Ser Val Val Arg
Thr Val Cys Leu Pro Pro Ala Asp Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu
Leu Ser Gly Tyr Gly Lys His Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Lys
Glu Ala His Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn
Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly Gly Pro
Gln Ala Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys
Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile Ser Trp Gly Leu Gly Cys Gly
Gln Lys Asp Val Pro Gly Val Tyr Thr Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg
Asp Asn Met

FIG. 64A

ATCACTCTCTTTAATCACTACTCACATTAACCTCAACTCCTGCCACAA
TGTACAGGATGCAACTCCTGTCTTGCATTGCACTAATTCTTGCACTTG
TCACAAACAGTGCACCTACTTCAAGTTCGACAAAGAAAACAAAGAAA
ACACAGCTACAACTGGAGCATTTACTGCTGGATTTACAGATGATTTTG
AATGGAATTAATAATTACAAGAATCCCAAACTCACCAGGATGCTCAC
ATTTAAGTTTTACATGCCCAAGAAGGCCACAGAACTGAAACAGCTTC
AGTGTCTAGAAGAAGAACTCAAACCTCTGGAGGAAGTGCTGAATTTA
GCTCAAAGCAAAAACTTTCACTTAAGACCCAGGGACTTAATCAGCAA
TATCAACGTAATAGTTCTGGAACTAAAGGGATCTGAAACAACATTCA
TGTGTGAATATGCAGATGAGACAGCAACCATTGTAGAATTTCTGAAC
AGATGGATTACCTTTTGTCAAAGCATCATCTCAACACTAACTTGATAA
TTAAGTGCTTCCCACTTAAAACATATCAGGCCTTCTATTTATTTATTTA
AATATTTAAATTTTATATTTATTGTTGAATGTATGGTTGCTACCTATTG
TAACTATTATTCTTAATCTTAAAACTATAAATATGGATCTTTTATGAT
TCTTTTTGTAAGCCCTAGGGGCTCTAAAATGGTTTACCTTATTTATCC
CAAAAATATTTATTATTATGTTGAATGTTAAATATAGTATCTATGTAG
ATTGGTTAGTAAAACTATTTAATAAATTTGATAAATATAAAAAAAAA
AAACAAAAAAAAAAA

FIG. 64B

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ile Leu Ala Leu Val Thr Asn
Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Lys Lys Thr Gln Leu Gln Leu Glu
His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys Asn
Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr
Glu Leu Lys Gln Leu Gln Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val
Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser
Asn Ile Asn Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu
Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys
Gln Ser Ile Ile Ser Thr Leu Thr

FIG. 65A-1

ATGCAAATAGAGCTCTCCACCTGCTTCTTTCTGTGCCTTTTGCGATTCT
GCTTTAGTGCCACCAGAAGATACTACCTGGGTGCAGTGGAACTGTCA
TGGGACTATATGCAAAGTGATCTCGGTGAGCTGCCTGTGGACGCAAG
ATTTCCTCCTAGAGTGCCAAAATCTTTTCCATTCAACACCTCAGTCGT
GTACAAAAAGACTCTGTTTGTAGAATTCACGGATCACCTTTTCAACAT
CGCTAAGCCAAGGCCACCCTGGATGGGTCTGCTAGGTCCTACCATCC
AGGCTGAGGTTTATGATACAGTGGTCATTACACTTAAGAACATGGCT
TCCCATCCTGTCAGTCTTCATGCTGTTGGTGTATCCTACTGGAAAGCT
TCTGAGGGAGCTGAATATGATGATCAGACCAGTCAAAGGGAGAAAG
AAGATGATAAAGTCTTCCCTGGTGGAAGCCATACATATGTCTGGCAG
GTCCTGAAAGAGAATGGTCCAATGGCCTCTGACCCACTGTGCCTTAC
CTACTCATATCTTTCTCATGTGGACCTGGTAAAAGACTTGAATTCAGG
CCTCATTGGAGCCCTACTAGTATGTAGAGAAGGGAGTCTGGCCAAGG
AAAAGACACAGACCTTGCACAAATTTATACTACTTTTTGCTGTATTTG
ATGAAGGGAAAAGTTGGCACTCAGAAACAAAGAACTCCTTGATGCA
GGATAGGGATGCTGCATCTGCTCGGGCCTGGCCTAAAATGCACACAG
TCAATGGTTATGTAAACAGGTCTCTGCCAGGTCTGATTGGATGCCACA
GGAAATCAGTCTATTGGCATGTGATTGGAATGGGCACCACTCCTGAA
GTGCACTCAATATTCCTCGAAGGTCACACATTTCTTGTGAGGAACCAT
CGCCAGGCGTCCTTGGAAATCTCGCCAATAACTTTCCTTACTGCTCAA
ACACTCTTGATGGACCTTGGACAGTTTCTACTGTTTTGTCATATCTCTT
CCCACCAACATGATGGCATGGAAGCTTATGTCAAAGTAGACAGCTGT
CCAGAGGAACCCCAACTACGAATGAAAAATAATGAAGAAGCGGAAG
ACTATGATGATGATCTTACTGATTCTGAAATGGATGTGGTCAGGTTTG
ATGATGACAACTCTCCTTCCTTTATCCAAATTCGCTCAGTTGCCAAGA
AGCATCCTAAAACTTGGGTACATTACATTGCTGCTGAAGAGGAGGAC
TGGGACTATGCTCCCTTAGTCCTCGCCCCCGATGACAGAAGTTATAAA
AGTCAATATTTGAACAATGGCCCTCAGCGGATTGGTAGGAAGTACAA
AAAAGTCCGATTTATGGCATACACAGATGAAACCTTTAAGACTCGTG
AAGCTATTCAGCATGAATCAGGAATCTTGGGACCTTTACTTTATGGGG
AAGTTGGAGACACACTGTTGATTATATTTAAGAATCAAGCAAGCAGA
CCATATAACATCTACCCTCACGGAATCACTGATGTCCGTCCTTTGTAT
TCAAGGAGATTACCAAAAGGTGTAAAACATTTGAAGGATTTTCCAAT
TCTGCCAGGAGAAATATTCAAATATAAATGGACAGTGACTGTAGAAG
ATGGGCCAACTAAATCAGATCCTCGGTGCCTGACCCGCTATTACTCTA
GTTTCGTTAATATGGAGAGAGATCTAGCTTCAGGACTCATTGGCCCTC
TCCTCATCTGCTACAAAGAATCTGTAGATCAAAGAGGAAACCAGATA
ATGTCAGACAAGAGGAATGTCATCCTGTTTTCTGTATTTGATGAGAAC
CGAAGCTGGTACCTCACAGAGAATATACAACGCTTTCTCCCCAATCCA
GCTGGAGTGCAGCTTGAGGATCCAGAGTTCCAAGCCTCCAACATCAT
GCACAGCATCAATGGCTATGTTTTTGATAGTTTGCAGTTGTCAGTTTG
TTTGCATGAGGTGGCATACTGGTACATTCTAAGCATTGGAGCACAGA
CTGACTTCCTTTCTGTCTTCTTCTCTGGATATACCTTCAAACACAAAAT

FIG. 65A-2

GGTCTATGAAGACACACTCACCCTATTCCCATTCTCAGGAGAAACTGT
CTTCATGTCGATGGAAAACCCAGGTCTATGGATTCTGGGGTGCCACA
ACTCAGACTTTCGGAACAGAGGCATGACCGCCTTACTGAAGGTTTCT
AGTTGTGACAAGAACACTGGTGATTATTACGAGGACAGTTATGAAGA
TATTTCAGCATACTTGCTGAGTAAAAACAATGCCATTGAACCAAGAA
GCTTCTCCCAGAATTCAAGACACCGTAGCACTAGGCAAAAGCAATTT
AATGCCACCACAATTCCAGAAAATGACATAGAGAAGACTGACCCTTG
GTTTGCACACAGAACACCTATGCCTAAAATACAAAATGTCTCCTCTA
GTGATTTGTTGATGCTCTTGCGACAGAGTCCTACTCCACATGGGCTAT
CCTTATCTGATCTCCAAGAAGCCAAATATGAGACTTTTTCTGATGATC
CATCACCTGGAGCAATAGACAGTAATAACAGCCTGTCTGAAATGACA
CACTTCAGGCCACAGCTCCATCACAGTGGGGACATGGTATTTACCCC
TGAGTCAGGCCTCCAATTAAGATTAAATGAGAAACTGGGGACAACTG
CAGCAACAGAGTTGAAGAAACTTGATTTCAAAGTTTCTAGTACATCA
AATAATCTGATTTCAACAATTCCATCAGACAATTTGGCAGCAGGTACT
GATAATACAAGTTCCTTAGGACCCCCAAGTATGCCAGTTCATTATGAT
AGTCAATTAGATACCACTCTATTTGGCAAAAAGTCATCTCCCCTTACT
GAGTCTGGTGGACCTCTGAGCTTGAGTGAAGAAAATAATGATTCAAA
GTTGTTAGAATCAGGTTTAATGAATAGCCAAGAAAGTTCATGGGGAA
AAAATGTATCGTCAACAGAGAGTGGTAGGTTATTTAAAGGGAAAAGA
GCTCATGGACCTGCTTTGTTGACTAAAGATAATGCCTTATTCAAAGTT
AGCATCTCTTTGTTAAAGACAAACAAAACTTCCAATAATTCAGCAACT
AATAGAAAGACTCACATTGATGGCCCATCATTATTAATTGAGAATAG
TCCATCAGTCTGGCAAAATATATTAGAAAGTGACACTGAGTTTAAAA
AAGTGACACCTTTGATTCATGACAGAATGCTTATGGACAAAAATGCT
ACAGCTTTGAGGCTAAATCATATGTCAAATAAAACTACTTCATCAAA
AAACATGGAAATGGTCCAACAGAAAAAAGAGGGCCCCATTCCACCA
GATGCACAAAATCCAGATATGTCGTTCTTTAAGATGCTATTCTTGCCA
GAATCAGCAAGGTGGATACAAAGGACTCATGGAAAGAACTCTCTGAA
CTCTGGGCAAGGCCCCAGTCCAAAGCAATTAGTATCCTTAGGACCAG
AAAAATCTGTGGAAGGTCAGAATTTCTTGTCTGAGAAAAACAAAGTG
GTAGTAGGAAAGGGTGAATTTACAAAGGACGTAGGACTCAAAGAGA
TGGTTTTTCCAAGCAGCAGAAACCTATTTCTTACTAACTTGGATAATT
TACATGAAAATAATACACACAATCAAGAAAAAAAAATTCAGGAAGA
AATAGAAAAGAAGGAAACATTAATCCAAGAGAATGTAGTTTTGCCTC
AGATACATACAGTGACTGGCACTAAGAATTTCATGAAGAACCTTTTC
TTACTGAGCACTAGGCAAAATGTAGAAGGTTCATATGACGGGGCATA
TGCTCCAGTACTTCAAGATTTTAGGTCATTAAATGATTCAACAAATAG
AACAAAGAAACACACAGCTCATTTCTCAAAAAAAGGGGAGGAAGAA
AACTTGGAAGGCTTGGGAAATCAAACCAGCAAATTGTAGAGAAATAT
GCATGCACCACAAGGAATATCTCCTAATACAAGCCAGCAGAATTTTG
TCACGCAACGTAGTAAGAGAGCTTTGAAACAATTCAGACTCCCACTA

FIG. 65A-3

GAAGAAACAGAACTTGAAAAAAGGATAATTGTGGATGACACCTCAAC
CCAGTGGTCCAAAAACATGAAACATTTGACCCCGAGCACCCTCACAC
AGATAGACTACAATGAGAAGGAGAAAGGGGCCATTACTCAGTCTCCC
TTATCAGATTGCCTTACGAGGAGTCATAGCATCCCTCAAGCAAATAGA
TCTCCATTACCCATTGCAAAGGTATCATCATTTCCATCTATTAGACCTA
TATATCTGACCAGGGTCCTATTCCAAGACAACTCTTCTCATCTTCCAG
CAGCATCTTATAGAAAGAAAGATTCTGGGGTCCAAGAAAGCAGTCAT
TTCTTACAAGGAGCCAAAAAAAATAACCTTTCTTTAGCCATTCTAACC
TTGGAGATGACTGGTGATCAAAGAGAGGTTGGCTCCCTGGGGACAAG
TGCCACAAATTCAGTCACATACAAGAAAGTTGAGAACACTGTTCTCCC
GAAACCAGACTTGCCCAAAACATCTGGCAAAGTTGAATTGCTTCCAA
AAGTTCACATTTATCAGAAGGACCTATTCCCTACGGAAACTAGCAATG
GGTCTCCTGGCCATCTGGATCTCGTGGAAGGGAGCCTTCTTCAGGGAA
CAGAGGGAGCGATTAAGTGGAATGAAGCAAACAGACCTGGAAAAGT
TCCCTTTCTGAGAGTAGCAACAGAAAGCTCTGCAAAGACTCCCTCCAA
GCTATTGGATCCTCTTGCTTGGGATAACCACTATGGTACTCAGATACC
AAAAGAAGAGTGGAAATCCCAAGAGAAGTCACCAGAAAAAACAGCT
TTTAAGAAAAAGGATACCATTTTGTCCCTGAACGCTTGTGAAAGCAAT
CATGCAATAGCAGCAATAAATGAGGGACAAAATAAGCCCGAAATAG
AAGTCACCTGGGCAAAGCAAGGTAGGACTGAAAGGCTGTGCTCTCAA
AACCCACCAGTCTTGAAACGCCATCAACGGGAAATAACTCGTACTAC
TCTTCAGTCAGATCAAGAGGAAATTGACTATGATGATACCATATCAGT
TGAAATGAAGAAGGAAGATTTTGACATTTATGATGAGGATGAAAATC
AGAGCCCCCGCAGCTTTCAAAAGAAAACACGACACTATTTTATTGCTG
CAGTGGAGAGGCTCTGGGATTATGGGATGAGTAGCTCCCCACATGTT
CTAAGAAACAGGGCTCAGAGTGGCAGTGTCCCTCAGTTCAAGAAAGT
TGTTTTCCAGGAATTTACTGATGGCTCCTTTACTCAGCCCTTATACCGT
GGAGAACTAAATGAACATTTGGGACTCCTGGGGCCATATATAAGAGC
AGAAGTTGAAGATAATATCATGGTAACTTTCAGAAATCAGGCCTCTC
GTCCCTATTCCTTCTATTCTAGCCTTATTTCTTATGAGGAAGATCAGAG
GCAAGGAGCAGAACCTAGAAAAAACTTTGTCAAGCCTAATGAAACCA
AAACTTACTTTTGGAAAGTGCAACATCATATGGCACCCACTAAAGAT
GAGTTTGACTGCAAAGCCTGGGCTTATTTCTCTGATGTTGACCTGGAA
AAAGATGTGCACTCAGGCCTGATTGGACCCCTTCTGGTCTGCCACACT
AACACACTGAACCCTGCTCATGGGAGACAAGTGACAGTACAGGAATT
TGCTCTGTTTTTCACCATCTTTGATGAGACCAAAAGCTGGTACTTCACT
GAAAATATGGAAAGAAACTGCAGGGCTCCCTGCAATATCCAGATGGA
AGATCCCACTTTTAAAGAGAATTATCGCTTCCATGCAATCAATGGCTA
CATAATGGATACACTACCTGGCTTAGTAATGGCTCAGGATCAAAGGA
TTCGATGGTATCTGCTCAGCATGGGCAGCAATGAAAACATCCATTCT
ATTCATTTCAGTGGACATGTGTTCACTGTACGAAAAAAAGAGGAGTA
TAAAATGGCACTGTACAATCTCTATCCAGGTGTTTTTGAGACAGTGGA

FIG. 65A-4

AATGTTACCATCCAAAGCTGGAATTTGGCGGGTGGAATGCCTTATTGG
CGAGCATCTACATGCTGGGATGAGCACACTTTTTCTGGTGTACAGCAA
TAAGTGTCAGACTCCCCTGGGAATGGCTTCTGGACACATTAGAGATTT
TCAGATTACAGCTTCAGGACAATATGGACAGTGGCCCCAAAGCTGG
CCAGACTTCATTATTCCGGATCAATCAATGCCTGGAGCACCAAGGAG
CCCTTTTCTTGGATCAAGGTGGATCTGTTGGCACCAATGATTATTCAC
GGCATCAAGACCCAGGGTGCCCGTCAGAAGTTCTCCAGCCTCTACAT
CTCTCAGTTTATCATCATGTATAGTCTTGATGGGAAGAAGTGGCAGA
CTTATCGAGGAAATTCCACTGGAACCTTAATGGTCTTCTTTGGCAATG
TGGATTCATCTGGGATAAAACACAATATTTTTAACCCTCCAATTATTG
CTCGATACATCCGTTTGCACCCAACTCATTATAGCATTCGCAGCACTC
TTCGCATGGAGTTGATGGGCTGTGATTTAAATAGTTGCAGCATGCCAT
TGGGAATGGAGAGTAAAGCAATATCAGATGCACAGATTACTGCTTCA
TCCTACTTTACCAATATGTTTGCCACCTGGTCTCCTTCAAAAGCTCGA
CTTCACCTCCAAGGGAGGAGTAATGCCTGGAGACCTCAGGTGAATAA
TCCAAAAGAGTGGCTGCAAGTGGACTTCCAGAAGACAATGAAAGTCA
CAGGAGTAACTACTCAGGGAGTAAAATCTCTGCTTACCAGCATGTAT
GTGAAGGAGTTCCTCATCTCCAGCAGTCAAGATGGCCATCAGTGGAC
TCTCTTTTTTCAGAATGGCAAAGTAAAGGTTTTTCAGGGAAATCAAGA
CTCCTTCACACCTGTGGTGAACTCTCTAGACCCACCGTTACTGACTCG
CTACCTTCGAATTCACCCCCAGAGTTGGGTGCACCAGATTGCCCTGAG
GATGGAGGTTCTGGGCTGCGAGGCACAGGACCTCTACTGAGGGTGGC
CACTGCAGCACCTGCCACTGCCGTCACCTCTCCCTCCTCAGCTCCAGG
GCAGTGTCCCTCCCTGGCTTGCCTTCTACCTTTGTGCTAAATCCTAGC
AGACACTGCCTTGAAGCCTCCTGAATTAACTATCATCAGTCCTGCATT
TCTTTGGTGGGGGGCCAGGAGGGTGCATCCAATTTAACTTAACTCTTA
CCTATTTTCTGCAGCTGCTCCCAGATTACTCCTTCCTTCCAATATAACT
AGGCAAAAAGAAGTGAGGAGAAACCTGCATGAAAGCATTCTTCCCTG
AAAAGTTAGGCCTCTCAGAGTCACCACTTCCTCTGTTGTAGAAAAACT
ATGTGATGAAACTTTGAAAAAGATATTTATGATGTTAACATTTCAGGT
TAAGCCTCATACGTTTAAAATAAAACTCTCAGTTGTTTATTATCCTGA
TCAAGCATGGAACAAAGCATGTTTCAGGATCAGATCAATACAATCTT
GGAGTCAAAAGGCAAATCATTTGGACAATCTGCAAAATGGAGAGAA
TACAATAACTACTACAGTAAAGTCTGTTTCTGCTTCCTTACACATAGA
TATAATTATGTTATTTAGTCATTATGAGGGGCACATTCTTATCTCCAA
AACTAGCATTCTTAAACTGAGAATTATAGATGGGGTTCAAGAATCCC
TAAGTCCCCTGAAATTATATAAGGCATTCTGTATAAATGCAAATGTGC
ATTTTTCTGACGAGTGTCCATAGATATAAAGCCATTTGGTCTTAATTCT
GACCAATAAAAAAATAAGTCAGGAGGATGCAATTGTTGAAAGCTTTG
AAATAAAATAACAATGTCTTCTTGAAATTTGTGATGGCCAAGAAAGA
AAATGATGA

FIG. 65B-1

Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe Cys Phe Ser
Ala Thr Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser Trp Asp Tyr Met Gln Ser
Asp Leu Gly Glu Leu Pro Val Asp Ala Arg Phe Pro Pro Arg Val Pro Lys Ser Phe
Pro Phe Asn Thr Ser Val Val Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Asp His
Leu Phe Asn Ile Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile
Gln Ala Glu Val Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser His Pro
Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser Glu Gly Ala Glu Tyr
Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp Asp Lys Val Phe Pro Gly Gly
Ser His Thr Tyr Val Trp Gln Val Leu Lys Glu Asn Gly Pro Met Ala Ser Asp Pro
Leu Cys Leu Thr Tyr Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn
Ser Gly Leu Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys
Thr Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly Lys Ser
Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp Ala Ala Ser Ala Arg
Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr Val Asn Arg Ser Leu Pro Gly Leu
Ile Gly Cys His Arg Lys Ser Val Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro
Glu Val His Ser Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln
Ala Ser Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met Asp
Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His Asp Gly Met Glu
Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln Leu Arg Met Lys Asn
Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp Leu Thr Asp Ser Glu Met Asp Val
Val Arg Phe Asp Asp Asp Asn Ser Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys
Lys His Pro Lys Thr Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr
Ala Pro Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn
Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met Ala Tyr Thr
Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu Ser Gly Ile Leu Gly Pro
Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile Ile Phe Lys Asn Gln Ala Ser
Arg Pro Tyr Asn Ile Tyr Pro His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg
Arg Leu Pro Lys Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile
Phe Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg
Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg Asp Leu Ala Ser
Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val Asp Gln Arg Gly Asn
Gln Ile Met Ser Asp Lys Arg Asn Val Ile Leu Phe Ser Val Phe Asp Glu Asn Arg
Ser Trp Tyr Leu Thr Glu Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln
Leu Glu Asp Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val
Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp Tyr Ile Leu
Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly Tyr Thr Phe Lys
His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe Pro Phe Ser Gly Glu Thr Val
Phe Met Ser Met Glu Asn Pro Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe
Arg Asn Arg Gly Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr
Gly Asp Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn
Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Ser Arg His Arg Ser Thr Arg Gln
Lys Gln Phe Asn Ala Thr Thr Ile Pro Glu Asn Asp Ile Glu Lys Thr Asp Pro Trp

FIG. 65B-2

Phe Ala His Arg Thr Pro Met Pro Lys Ile Gln Asn Val Ser Ser Ser Asp Leu Leu
Met Leu Leu Arg Gln Ser Pro Thr Pro His Gly Leu Ser Leu Ser Asp Leu Gln Glu
Ala Lys Tyr Glu Thr Phe Ser Asp Asp Pro Ser Pro Gly Ala Ile Asp Ser Asn Asn
Ser Leu Ser Glu Met Thr His Phe Arg Pro Gln Leu His His Ser Gly Asp Met Val
Phe Thr Pro Glu Ser Gly Leu Gln Leu Arg Leu Asn Glu Lys Leu Gly Thr Thr
Ala Ala Thr Glu Leu Lys Lys Leu Asp Phe Lys Val Ser Ser Thr Ser Asn Asn Leu
Ile Ser Thr Ile Pro Ser Asp Asn Leu Ala Ala Gly Thr Asp Asn Thr Ser Ser Leu
Gly Pro Pro Ser Met Pro Val His Tyr Asp Ser Gln Leu Asp Thr Thr Leu Phe Gly
Lys Lys Ser Ser Pro Leu Thr Glu Ser Gly Gly Pro Leu Ser Leu Ser Glu Glu Asn
Asn Asp Ser Lys Leu Leu Glu Ser Gly Leu Met Asn Ser Gln Glu Ser Ser Trp Gly
Lys Asn Val Ser Ser Thr Glu Ser Gly Arg Leu Phe Lys Gly Lys Arg Ala His Gly
Pro Ala Leu Leu Thr Lys Asp Asn Ala Leu Phe Lys Val Ser Ile Ser Leu Leu
Lys Thr Asn Lys Thr Ser Asn Asn Ser Ala Thr Asn Arg Lys Thr His Ile Asp
Gly Pro Ser Leu Leu Ile Glu Asn Ser Pro Ser Val Trp Gln Asn Ile Leu Glu Ser
Asp Thr Glu Phe Lys Lys Val Thr Pro Leu Ile His Asp Arg Met Leu Met Asp
Lys Asn Ala Thr Ala Leu Arg Leu Asn His Met Ser Asn Lys Thr Thr Ser Ser
Lys Asn Met Glu Met Val Gln Gln Lys Lys Glu Gly Pro Ile Pro Pro Asp Ala
Gln Asn Pro Asp Met Ser Phe Phe Lys Met Leu Phe Leu Pro Glu Ser Ala Arg
Trp Ile Gln Arg Thr His Gly Lys Asn Ser Leu Asn Ser Gly Gln Gly Pro Ser Pro
Lys Gln Leu Val Ser Leu Gly Pro Glu Lys Ser Val Glu Gly Gln Asn Phe Leu
Ser Glu Lys Asn Lys Val Val Val Gly Lys Gly Glu Phe Thr Lys Asp Val Gly
Leu Lys Glu Met Val Phe Pro Ser Ser Arg Asn Leu Phe Leu Thr Asn Leu Asp
Asn Leu His Glu Asn Asn Thr His Asn Gln Glu Lys Lys Ile Gln Glu Glu Ile
Glu Lys Lys Glu Thr Leu Ile Gln Glu Asn Val Val Leu Pro Gln Ile His Thr
Val Thr Gly Thr Lys Asn Phe Met Lys Asn Leu Phe Leu Leu Ser Thr Arg Gln
Asn Val Glu Gly Ser Tyr Asp Gly Ala Tyr Ala Pro Val Leu Gln Asp Phe Arg
Ser Leu Asn Asp Ser Thr Asn Arg Thr Lys Lys His Thr Ala His Phe Ser Lys
Lys Gly Glu Glu Glu Asn Leu Glu Gly Leu Gly Asn Gln Thr Lys Gln Ile Val
Glu Lys Tyr Ala Cys Thr Thr Arg Ile Ser Pro Asn Thr Ser Gln Gln Asn Phe
Val Thr Gln Arg Ser Lys Arg Ala Leu Lys Gln Phe Arg Leu Pro Leu Glu Glu
Thr Glu Leu Glu Lys Arg Ile Ile Val Asp Asp Thr Ser Thr Gln Trp Ser Lys Asn
Met Lys His Leu Thr Pro Ser Thr Leu Thr Gln Ile Asp Tyr Asn Glu Lys Glu
Lys Gly Ala Ile Thr Gln Ser Pro Leu Ser Asp Cys Leu Thr Arg Ser His Ser Ile
Pro Gln Ala Asn Arg Ser Pro Leu Pro Ile Ala Lys Val Ser Ser Phe Pro Ser Ile
Arg Pro Ile Tyr Leu Thr Arg Val Leu Phe Gln Asp Asn Ser Ser His Leu Pro
Ala Ala Ser Tyr Arg Lys Lys Asp Ser Gly Val Gln Glu Ser Ser His Phe Leu
Gln Gly Ala Lys Lys Asn Asn Leu Ser Leu Ala Ile Leu Thr Leu Glu Met Thr
Gly Asp Gln Arg Glu Val Gly Ser Leu Gly Thr Ser Ala Thr Asn Ser Val Thr
Tyr Lys Lys Val Glu Asn Thr Val Leu Pro Lys Pro Asp Leu Pro Lys Thr Ser
Gly Lys Val Glu Leu Leu Pro Lys Val His Ile Tyr Gln Lys Asp Leu Phe Pro
Thr Glu Thr Ser Asn Gly Ser Pro Gly His Leu Asp Leu Val Glu Gly Ser Leu

FIG. 65B-3

Leu Gln Gly Thr Glu Gly Ala Ile Lys Trp Asn Glu Ala Asn Arg Pro Gly Lys
Val Pro Phe Leu Arg Val Ala Thr Glu Ser Ser Ala Lys Thr Pro Ser Lys Leu
Leu Asp Pro Leu Ala Trp Asp Asn His Tyr Gly Thr Gln Ile Pro Lys Glu Glu
Trp Lys Ser Gln Glu Lys Ser Pro Glu Lys Thr Ala Phe Lys Lys Lys Asp Thr Ile
Leu Ser Leu Asn Ala Cys Glu Ser Asn His Ala Ile Ala Ala Ile Asn Glu Gly
Gln Asn Lys Pro Glu Ile Glu Val Thr Trp Ala Lys Gln Gly Arg Thr Glu Arg
Leu Cys Ser Gln Asn Pro Pro Val Leu Lys Arg His Gln Arg Glu Ile Thr Arg
Thr Thr Leu Gln Ser Asp Gln Glu Glu Ile Asp Tyr Asp Asp Thr Ile Ser Val Glu
Met Lys Lys Glu Asp Phe Asp Ile Tyr Asp Glu Asp Glu Asn Gln Ser Pro Arg
Ser Phe Gln Lys Lys Thr Arg His Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp Asp
Tyr Gly Met Ser Ser Ser Pro His Val Leu Arg Asn Arg Ala Gln Ser Gly Ser Val
Pro Gln Phe Lys Lys Val Val Phe Gln Glu Phe Thr Asp Gly Ser Phe Thr Gln Pro
Leu Tyr Arg Gly Glu Leu Asn Glu His Leu Gly Leu Leu Gly Pro Tyr Ile Arg
Ala Glu Val Glu Asp Asn Ile Met Val Thr Phe Arg Asn Gln Ala Ser Arg Pro
Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Glu Glu Asp Gln Arg Gln Gly Ala Glu
Pro Arg Lys Asn Phe Val Lys Pro Asn Glu Thr Lys Thr Tyr Phe Trp Lys Val
Gln His His Met Ala Pro Thr Lys Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr
Phe Ser Asp Val Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly Pro Leu
Leu Val Cys His Thr Asn Thr Leu Asn Pro Ala His Gly Arg Gln Val Thr Val Gln
Glu Phe Ala Leu Phe Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp Tyr Phe Thr Glu
Asn Met Glu Arg Asn Cys Arg Ala Pro Cys Asn Ile Gln Met Glu Asp Pro Thr
Phe Lys Glu Asn Tyr Arg Phe His Ala Ile Asn Gly Tyr Ile Met Asp Thr Leu Pro
Gly Leu Val Met Ala Gln Asp Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly
Ser Asn Glu Asn Ile His Ser Ile His Phe Ser Gly His Val Phe Thr Val Arg Lys
Lys Glu Glu Tyr Lys Met Ala Leu Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr
Val Glu Met Leu Pro Ser Lys Ala Gly Ile Trp Arg Val Glu Cys Leu Ile Gly Glu
His Leu His Ala Gly Met Ser Thr Leu Phe Leu Val Tyr Ser Asn Lys Cys Gln Thr
Pro Leu Gly Met Ala Ser Gly His Ile Arg Asp Phe Gln Ile Thr Ala Ser Gly Gln
Tyr Gly Gln Trp Ala Pro Lys Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala
Trp Ser Thr Lys Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile
Ile His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr Ile Ser
Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln Thr Tyr Arg Gly
Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn Val Asp Ser Ser Gly Ile
Lys His Asn Ile Phe Asn Pro Pro Ile Ile Ala Arg Tyr Ile Arg Leu His Pro Thr
His Tyr Ser Ile Arg Ser Thr Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn
Ser Cys Ser Met Pro Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr
Ala Ser Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala Arg Leu
His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro Gln Val Asn Asn Pro Lys Glu
Trp Leu Gln Val Asp Phe Gln Lys Thr Met Lys Val Thr Gly Val Thr Thr Gln
Gly Val Lys Ser Leu Leu Thr Ser Met Tyr Val Lys Glu Phe Leu Ile Ser Ser Ser
Gln Asp Gly His Gln Trp Thr Leu Phe Phe Gln Asn Gly Lys Val Lys Val Phe
Gln Gly Asn Gln Asp Ser Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu
Leu Thr Arg Tyr Leu Arg Ile His

FIG.65B-4

Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg Met Glu Val Leu Gly Cys Glu
Ala Gln Asp Leu Tyr

FIG. 66A

TCCACCTGTCCCCGCAGCGCCGGCTCGCGCCCTCCTGCCGCAGCCACC
GAGCCGCCGTCTAGCGCCCCGACCTCGCCACCATGAGAGCCCTGCTG
GCGCGCCTGCTTCTCTGCGTCCTGGTCGTGAGCGACTCCAAAGGCAGC
AATGAACTTCATCAAGTTCCATCGAACTGTGACTGTCTAAATGGAGGA
ACATGTGTGTCCAACAAGTACTTCTCCAACATTCACTGGTGCAACTGC
CCAAAGAAATTCGGAGGGCAGCACTGTGAAATAGATAAGTCAAAAAC
CTGCTATGAGGGGAATGGTCACTTTTACCGAGGAAAGGCCAGCACTG
ACACCATGGGCCGGCCCTGCCTGCCCTGGAACTCTGCCACTGTCCTTC
AGCAAACGTACCATGCCCACAGATCTGATGCTCTTCAGCTGGGCCTGG
GGAAACATAATTACTGCAGGAACCCAGACAACCGGAGGCGACCCTGG
TGCTATGTGCAGGTGGGCCTAAAGCCGCTTGTCCAAGAGTGCATGGT
GCATGACTGCGCAGATGGAAAAAAGCCCTCCTCTCCTCCAGAAGAAT
TAAAATTTCAGTGTGGCCAAAAGACTCTGAGGCCCCGCTTTAAGATTA
TTGGGGGAGAATTCACCACCATCGAGAACCAGCCCTGGTTTGCGGCC
ATCTACAGGAGGCACCGGGGGGGCTCTGTCACCTACGTGTGTGGAGG
CAGCCTCATCAGCCCTTGCTGGGTGATCAGCGCCACACACTGCTTCAT
TGATTACCCAAAGAAGGAGGACTACATCGTCTACCTGGGTCGCTCAA
GGCTTAACTCCAACACGCAAGGGGAGATGAAGTTTGAGGTGGAAAAC
CTCATCCTACACAAGGACTACAGCGCTGACACGCTTGCTCACCACAAC
GACATTGCCTTGCTGAAGATCCGTTCCAAGGAGGGCAGGTGTGCGCA
GCCATCCCGGACTATACAGACCATCTGCCTGCCCTCGATGTATAACGA
TCCCCAGTTTGGCACAAGCTGTGAGATCACTGGCTTTGGAAAAGAGA
ATTCTACCGACTATCTCTATCCGGAGCAGCTGAAGATGACTGTTGTGA
AGCTGATTTCCCACCGGGAGTGTCAGCAGCCCCACTACTACGGCTCTG
AAGTCACCACCAAAATGCTGTGTGCTGCTGACCCACAGTGGAAAACA
GATTCCTGCCAGGGAGACTCAGGGGGACCCCTCGTCTGTTCCCTCCAA
GGCCGCATGACTTTGACTGGAATTGTGAGCTGGGGCCGTGGATGTGC
CCTGAAGGACAAGCCAGGCGTCTACACGAGAGTCTCACACTTCTTAC
CCTGGATCCGCAGTCACACCAAGGAAGAGAATGGCCTGGCCCTCTGA
GGGTCCCCAGGGAGGAAACGGGCACCACCCGCTTTCTTGCTGGTTGTC
ATTTTTGCAGTAGAGTCATCTCCATCAGCTGTAAGAAGAGACTGGGA
AGAT

FIG. 66B

Met Arg Ala Leu Leu Ala Arg Leu Leu Leu Cys Val Leu Val Val Ser Asp Ser
Lys Gly Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp Cys Leu Asn Gly
Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile His Trp Cys Asn Cys Pro Lys
Lys Phe Gly Gly Gln His Cys Glu Ile Asp Lys Ser Lys Thr Cys Tyr Glu Gly Asn
Gly His Phe Tyr Arg Gly Lys Ala Ser Thr Asp Thr Met Gly Arg Pro Cys Leu Pro
Trp Asn Ser Ala Thr Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu
Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg Arg Arg
Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln Glu Cys Met Val His
Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro Pro Glu Glu Leu Lys Phe Gln Cys
Gly Gln Lys Thr Leu Arg Pro Arg Phe Lys Ile Ile Gly Gly Glu Phe Thr Thr Ile
Glu Asn Gln Pro Trp Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr
Tyr Val Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys
Phe Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser Arg Leu
Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn Leu Ile Leu His Lys
Asp Tyr Ser Ala Asp Thr Leu Ala His His Asn Asp Ile Ala Leu Leu Lys Ile Arg
Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro
Ser Met Tyr Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys
Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr Thr
Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys Gln Gly Asp
Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met Thr Leu Thr Gly Ile Val
Ser Trp Gly Arg Gly Cys Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser
His Phe Leu Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu

FIG.67A

TCCTGCACAGGCAGTGCCTTGAAGTGCTTCTTCAGAGACCTTTCTTCA
TAGACTACTTTTTTTCTTTAAGCAGCAAAAGGAGAAAATTGTCATCA
AGGATATTCCAGATTCTTGACAGCATTCTCGTCATCTCTGAGGACATC
ACCATCATCTCAGGATGAGGGGCATGAAGCTGCTGGGGGCGCTGCTG
GCACTGGCGGCCCTACTGCAGGGGGCCGTGTCCCTGAAGATCGCAGC
CTTCAACATCCAGACATTTGGGGAGACCAAGATGTCCAATGCCACCCT
CGTCAGCTACATTGTGCAGATCCTGAGCCGCTATGACATCGCCCTGGT
CCAGGAGGTCAGAGACAGCCACCTGACTGCCGTGGGGAAGCTGCTGG
ACAACCTCAATCAGGATGCACCAGACACCTATCACTACGTGGTCAGT
GAGCCACTGGGACGGAACAGCTATAAGGAGCGCTACCTGTTCGTGTA
CAGGCCTGACCAGGTGTCTGCGGTGGACAGCTACTACTACGATGATG
GCTGCGAGCCCTGCGGGAACGACACCTTCAACCGAGAGCCAGCCATT
GTCAGGTTCTTCTCCCGGTTCACAGAGGTCAGGGAGTTTGCCATTGTT
CCCCTGCATGCGGCCCCGGGGGACGCAGTAGCCGAGATCGACGCTCT
CTATGACGTCTACCTGGATGTCCAAGAGAAATGGGGCTTGGAGGACG
TCATGTTGATGGGCGACTTCAATGCGGGCTGCAGCTATGTGAGACCCT
CCCAGTGGTCATCCATCCGCCTGTGGACAAGCCCCACCTTCCAGTGGC
TGATCCCCGACAGCGCTGACACCACAGCTACACCCACGCACTGTGCCT
ATGACAGGATCGTGGTTGCAGGGATGCTGCTCCGAGGCGCCGTTGTTC
CCGACTCGGCTCTTCCCTTTAACTTCCAGGCTGCCTATGGCCTGAGTG
ACCAACTGGCCCAAGCCATCAGTGACCACTATCCAGTGGAGGTGATG
CTGAAGTGAGCAGCCCCTCCCCACACCAGTTGAACTGCAG

FIG. 67B

Met Arg Gly Met Lys Leu Leu Gly Ala Leu Leu Ala Leu Ala Ala Leu Leu Gln
Gly Ala Val Ser Leu Lys Ile Ala Ala Phe Asn Ile Gln Thr Phe Gly Glu Thr Lys
Met Ser Asn Ala Thr Leu Val Ser Tyr Ile Val Gln Ile Leu Ser Arg Tyr Asp Ile
Ala Leu Val Gln Glu Val Arg Asp Ser His Leu Thr Ala Val Gly Lys Leu Leu
Asp Asn Leu Asn Gln Asp Ala Pro Asp Thr Tyr His Tyr Val Val Ser Glu Pro
Leu Gly Arg Asn Ser Tyr Lys Glu Arg Tyr Leu Phe Val Tyr Arg Pro Asp Gln
Val Ser Ala Val Asp Ser Tyr Tyr Tyr Asp Asp Gly Cys Glu Pro Cys Gly Asn
Asp Thr Phe Asn Arg Glu Pro Ala Ile Val Arg Phe Phe Ser Arg Phe Thr Glu Val
Arg Glu Phe Ala Ile Val Pro Leu His Ala Ala Pro Gly Asp Ala Val Ala Glu Ile
Asp Ala Leu Tyr Asp Val Tyr Leu Asp Val Gln Glu Lys Trp Gly Leu Glu Asp
Val Met Leu Met Gly Asp Phe Asn Ala Gly Cys Ser Tyr Val Arg Pro Ser Gln
Trp Ser Ser Ile Arg Leu Trp Thr Ser Pro Thr Phe Gln Trp Leu Ile Pro Asp Ser
Ala Asp Thr Thr Ala Thr Pro Thr His Cys Ala Tyr Asp Arg Ile Val Val Ala Gly
Met Leu Leu Arg Gly Ala Val Val Pro Asp Ser Ala Leu Pro Phe Asn Phe Gln
Ala Ala Tyr Gly Leu Ser Asp Gln Leu Ala Gln Ala Ile Ser Asp His Tyr Pro Val
Glu Val Met Leu Lys

FIG. 68A

GCTGCATCAGAAGAGGCCATCAAGCACATCACTGTCCTTCTGCCATGG
CCCTGTGGATGCGCCTCCTGCCCCTGCTGGCGCTGCTGGCCCTCTGGG
GACCTGACCCAGCCGCAGCCTTTGTGAACCAACACCTGTGCGGCTCAC
ACCTGGTGGAAGCTCTCTACCTAGTGTGCGGGGAACGAGGCTTCTTCT
ACACACCCAAGACCCGCCGGGAGGCAGAGGACCTGCAGGTGGGGCA
GGTGGAGCTGGGCGGGGGCCCTGGTGCAGGCAGCCTGCAGCCCTTGG
CCCTGGAGGGGTCCCTGCAGAAGCGTGGCATTGTGGAACAATGCTGT
ACCAGCATCTGCTCCCTCTACCAGCTGGAGAACTACTGCAACTAGACG
CAGCCCGCAGGCAGCCCCCCACCCGCCGCCTCCTGCACCGAGAGAGA
TGGAATAAAGCCCTTGAACCAGC

FIG. 68B

Met Ala Leu Trp Met Arg Leu Leu Pro Leu Leu Ala Leu Leu Ala Leu Trp Gly
Pro Asp Pro Ala Ala Ala Phe Val Asn Gln His Leu Cys Gly Ser His Leu Val
Glu Ala Leu Tyr Leu Val Cys Gly Glu Arg Gly Phe Phe Tyr Thr Pro Lys Thr
Arg Arg Glu Ala Glu Asp Leu Gln Val Gly Gln Val Glu Leu Gly Gly Gly Pro
Gly Ala Gly Ser Leu Gln Pro Leu Ala Leu Glu Gly Ser Leu Gln Lys Arg Gly Ile
Val Glu Gln Cys Cys Thr Ser Ile Cys Ser Leu Tyr Gln Leu Glu Asn Tyr Cys Asn

FIG. 69A

ATGGGAGGTTGGTCTTCCAAACCTCGACAAGGCATGGGGACGAATCT
TTCTGTTCCCAATCCTCTGGGATTCTTTCCCGATCACCAGTTGGACCCT
GCGTTCGGAGCCAACTCAAACAATCCAGATTGGGACTTCAACCCCAA
CAAGGATCACTGGCCAGAGGCAATCAAGGTAGGAGCGGGAGACTTC
GGGCCAGGGTTCACCCCACCACACGGCGGTCTTTTGGGGTGGAGCCC
TCAGGCTCAGGGCATATTGACAACAGTGCCAGCAGCGCCTCCTCCTG
TTTCCACCAATCGGCAGTCAGGAAGACAGCCTACTCCCATCTCTCCAC
CTCTAAGAGACAGTCATCCTCAGGCCATGCAGTGGAACTCCACAACA
TTCCACCAAGCTCTGCTAGATCCCAGAGTGAGGGGCCTATATTTTCCT
GCTGGTGGCTCCAGTTCCGGAACAGTAAACCCTGTTCCGACTACTGTC
TCACCCATATCGTCAATCTTCTCGAGGACTGGGGACCCTGCACCGAAC
ATGGAGAGCACAACATCAGGATTCCTAGGACCCCTGCTCGTGTTACA
GGCGGGGTTTTTCTTGTTGACAAGAATCCTCACAATACCACAGAGTCT
AGACTCGTGGTGGACTTCTCTCAATTTTCTAGGGGGAGCACCCACGTG
TCCTGGCCAAAATTCGCAGTCCCCAACCTCCAATCACTCACCAACCTC
TTGTCCTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTTT
ATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTGTTGGTTC
TTCTGGACTACCAAGGTATGTTGCCCGTTTGTCCTCTACTTCCAGGAA
CATCAACTACCAGCACGGGACCATGCAAGACCTGCACGATTCCTGCT
CAAGGAACCTCTATGTTTCCCTCTTGTTGCTGTACAAAACCTTCGGAC
GGAAACTGCACTTGTATTCCCATCCCATCATCCTGGGCTTTCGCAAGA
TTCCTATGGGAGTGGGCCTCAGTCCGTTTCTCCTGGCTCAGTTTACTA
GTGCCATTTGTTCAGTGGTTCGCAGGGCTTTCCCCCACTGTTTGGCTTT
CAGTTATATGGATGATGTGGTATTGGGGGCCAAGTCTGTACAACATCT
TGAGTCCCTTTTTACCTCTATTACCAATTTTCTTTTGTCTTTGGGTATAC
ATTTGA

FIG. 69B

Met Gly Gly Trp Ser Ser Lys Pro Arg Gln Gly Met Gly Thr Asn Leu Ser Val Pro
Asn Pro Leu Gly Phe Phe Pro Asp His Gln Leu Asp Pro Ala Phe Gly Ala Asn
Ser Asn Asn Pro Asp Trp Asp Phe Asn Pro Asn Lys Asp His Trp Pro Glu Ala Ile
Lys Val Gly Ala Gly Asp Phe Gly Pro Gly Phe Thr Pro Pro His Gly Gly Leu Leu
Gly Trp Ser Pro Gln Ala Gln Gly Ile Leu Thr Thr Val Pro Ala Ala Pro Pro Pro
Val Ser Thr Asn Arg Gln Ser Gly Arg Gln Pro Thr Pro Ile Ser Pro Pro Leu Arg
Asp Ser His Pro Gln Ala Met Gln Trp Asn Ser Thr Thr Phe His Gln Ala Leu Leu
Asp Pro Arg Val Arg Gly Leu Tyr Phe Pro Ala Gly Gly Ser Ser Ser Gly Thr Val
Asn Pro Val Pro Thr Thr Val Ser Pro Ile Ser Ser Ile Phe Ser Arg Thr Gly Asp
Pro Ala Pro Asn Met Glu Ser Thr Thr Ser Gly Phe Leu Gly Pro Leu Leu Val Leu
Gln Ala Gly Phe Phe Leu Leu Thr Arg Ile Leu Thr Ile Pro Gln Ser Leu Asp Ser
Trp Trp Thr Ser Leu Asn Phe Leu Gly Gly Ala Pro Thr Cys Pro Gly Gln Asn Ser
Gln Ser Pro Thr Ser Asn His Ser Pro Thr Ser Cys Pro Pro Ile Cys Pro Gly Tyr
Arg Trp Met Cys Leu Arg Arg Phe Ile Ile Phe Leu Phe Ile Leu Leu Leu Cys Leu
Ile Phe Leu Leu Val Leu Leu Asp Tyr Gln Gly Met Leu Pro Val Cys Pro Leu
Leu Pro Gly Thr Ser Thr Thr Ser Thr Gly Pro Cys Lys Thr Cys Thr Ile Pro Ala
Gln Gly Thr Ser Met Phe Pro Ser Cys Cys Cys Thr Lys Pro Ser Asp Gly Asn
Cys Thr Cys Ile Pro Ile Pro Ser Ser Trp Ala Phe Ala Arg Phe Leu Trp Glu Trp
Ala Ser Val Arg Phe Ser Trp Leu Ser Leu Leu Val Pro Phe Val Gln Trp Phe Ala
Gly Leu Ser Pro Thr Val Trp Leu Ser Val Ile Trp Met Met Trp Tyr Trp Gly Pro
Ser Leu Tyr Asn Ile Leu Ser Pro Phe Leu Pro Leu Leu Pro Ile Phe Phe Cys Leu
Trp Val Tyr Ile

FIG. 70A

CGAACCACTCAGGGTCCTGTGGACAGCTCACCTAGCTGCAATGGCTA
CAGGCTCCCGGACGTCCCTGCTCCTGGCTTTTGGCCTGCTCTGCCTGC
CCTGGCTTCAAGAGGGCAGTGCCTTCCCAACCATTCCCTTATCCAGGC
CTTTTGACAACGCTATGCTCCGCGCCCATCGTCTGCACCAGCTGGCCT
TTGACACCTACCAGGAGTTTGAAGAAGCCTATATCCCAAAGGAACAG
AAGTATTCATTCCTGCAGAACCCCCAGACCTCCCTCTGTTTCTCAGAG
TCTATTCCGACACCCTCCAACAGGGAGGAAACACAACAGAAATCCAA
CCTAGAGCTGCTCCGCATCTCCCTGCTGCTCATCCAGTCGTGGCTGGA
GCCCGTGCAGTTCCTCAGGAGTGTCTTCGCCAACAGCCTGGTGTACGG
CGCCTCTGACAGCAACGTCTATGACCTCCTAAAGGACCTAGAGGAAG
GCATCCAAACGCTGATGGGGAGGCTGGAAGATGGCAGCCCCCGGACT
GGGCAGATCTTCAAGCAGACCTACAGCAAGTTCGACACAAACTCACA
CAACGATGACGCACTACTCAAGAACTACGGGCTGCTCTACTGCTTCAG
GAAGGACATGGCAAGGTCGAGACATTCCTGCGCATCGTGCAGTGCCG
CTCTGTGGAGGGCAGCTGTGGCTTCTAGCTGCCCGGGTGGCATCCCTG
TGACCCCTCCCCAGTGCCTCTCCTGGCCCTGGAAGTTGCCACTCCAGT
GCCCACCAGCCTTGTCCTAATAAAATTAAGTTGCATC

FIG. 70B

Met Ala Thr Gly Ser Arg Thr Ser Leu Leu Leu Ala Phe Gly Leu Leu Cys Leu
Pro Trp Leu Gln Glu Gly Ser Ala Phe Pro Thr Ile Pro Leu Ser Arg Pro Phe Asp
Asn Ala Met Leu Arg Ala His Arg Leu His Gln Leu Ala Phe Asp Thr Tyr Gln
Glu Phe Glu Glu Ala Tyr Ile Pro Lys Glu Gln Lys Tyr Ser Phe Leu Gln Asn Pro
Gln Thr Ser Leu Cys Phe Ser Glu Ser Ile Pro Thr Pro Ser Asn Arg Glu Glu Thr
Gln Gln Lys Ser Asn Leu Glu Leu Leu Arg Ile Ser Leu Leu Leu Ile Gln Ser Trp
Leu Glu Pro Val Gln Phe Leu Arg Ser Val Phe Ala Asn Ser Leu Val Tyr Gly Ala
Ser Asp Ser Asn Val Tyr Asp Leu Leu Lys Asp Leu Glu Glu Gly Ile Gln Thr Leu
Met Gly Arg Leu Glu Asp Gly Ser Pro Arg Thr Gly Gln Ile Phe Lys Gln Thr Tyr
Ser Lys Phe Asp Thr Asn Ser His Asn Asp Asp Ala Leu Leu Lys Asn Tyr Gly
Leu Leu Tyr Cys Phe Arg Lys Asp Met Asp Lys Val Glu Thr Phe Leu Arg Ile
Val Gln CysArg Ser Val Glu Gly Ser Cys Gly Phe

FIG. 71A

ATGGCGCCCGTCGCCGTCTGGGCCGCGCTGGCCGTCGGACTGGAGCT
CTGGGCTGCGGCGCACGCCTTGCCCGCCCAGGTGGCATTTACACCCTA
CGCCCCGGAGCCCGGGAGCACATGCCGGCTCAGAGAATACTATGACC
AGACAGCTCAGATGTGCTGCAGCAAATGCTCGCCGGGCCAACATGCA
AAAGTCTTCTGTACCAAGACCTCGGACACCGTGTGTGACTCCTGTGAG
GACAGCACATACACCCAGCTCTGGAACTGGGTTCCCGAGTGCTTGAG
CTGTGGCTCCCGCTGTAGCTCTGACCAGGTGGAAACTCAAGCCTGCAC
TCGGGAACAGAACCGCATCTGCACCTGCAGGCCCGGCTGGTACTGCG
CGCTGAGCAAGCAGGAGGGGTGCCGGCTGTGCGCGCCGCTGCGCAAG
TGCCGCCCGGGCTTCGGCGTGGCCAGACCAGGAACTGAAACATCAGA
CGTGGTGTGCAAGCCCTGTGCCCCGGGGACGTTCTCCAACACGACTTC
ATCCACGGATATTTGCAGGCCCCACCAGATCTGTAACGTGGTGGCCAT
CCCTGGGAATGCAAGCATGGATGCAGTCTGCACGTCCACGTCCCCCA
CCCGGAGTATGGCCCCAGGGGCAGTACACTTACCCCAGCCAGTGTCC
ACACGATCCCAACACACGCAGCCAACTCCAGAACCCAGCACTGCTCC
AAGCACCTCCTTCCTGCTCCCAATGGGCCCCAGCCCCCCAGCTGAAGG
GAGCACTGGCGACTTCGCTCTTCCAGTTGGACTGATTGTGGGTGTGAC
AGCCTTGGGTCTACTAATAATAGGAGTGGTGAACTGTGTCATCATGAC
CCAGGTGAAAAAGAAGCCCTTGTGCCTGCAGAGAGAAGCCAAGGTGC
CTCACTTGCCTGCCGATAAGGCCCGGGGTACACAGGGCCCCGAGCAG
CAGCACCTGCTGATCACAGCGCCGAGCTCCAGCAGCAGCTCCCTGGA
GAGCTCGGCCAGTGCGTTGGACAGAAGGGCGCCCACTCGGAACCAGC
CACAGGCACCAGGCGTGGAGGCCAGTGGGGCCGGGGAGGCCCGGGC
CAGCACCGGGAGCTCAGATTCTTCCCCTGGTGGCCATGGGACCCAGG
TCAATGTCACCTGCATCGTGAACGTCTGTAGCAGCTCTGACCACAGCT
CACAGTGCTCCTCCCAAGCCAGCTCCACAATGGGAGACACAGATTCC
AGCCCCTCGGAGTCCCCGAAGGACGAGCAGGTCCCCTTCTCCAAGGA
GGAATGTGCCTTTCGGTCACAGCTGGAGACGCCAGAGACCCTGCTGG
GGAGCACCGAAGAGAAGCCCCTGCCCCTTGGAGTGCCTGATGCTGGG
ATGAAGCCCAGTTAACCAGGCCGGTGTGGGCTGTGTCGTAGCCAAGG
TGGGCTGAGCCCTGGCAGGATGACCCTGCGAAGGGGCCCTGGTCCTT
CCAGGC

FIG. 71B

Met Ala Pro Val Ala Val Trp Ala Ala Leu Ala Val Gly Leu Glu Leu Trp Ala Ala
Ala His Ala Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr Ala Pro Glu Pro Gly Ser
Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln Thr Ala Gln Met Cys Cys Ser Lys
Cys Ser Pro Gly Gln His Ala Lys Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys
Asp Ser Cys Glu Asp Ser Thr Tyr Thr Gln Leu Trp Asn Trp Val Pro Glu Cys
Leu Ser Cys Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg
Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu Ser Lys Gln
Glu Gly Cys Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg Pro Gly Phe Gly Val
Ala Arg Pro Gly Thr Glu Thr Ser Asp Val Val Cys Lys Pro Cys Ala Pro Gly Thr
Phe Ser Asn Thr Thr Ser Ser Thr Asp Ile Cys Arg Pro His Gln Ile Cys Asn Val
Val Ala Ile Pro Gly Asn Ala Ser Met Asp Ala Val Cys Thr Ser Thr Ser Pro Thr
Arg Ser Met Ala Pro Gly Ala Val His Leu Pro Gln Pro Val Ser Thr Arg Ser Gln
His Thr Gln Pro Thr Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser Phe Leu Leu Pro
Met Gly Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly Asp Phe Ala Leu Pro Val Gly
Leu Ile Val Gly Val Thr Ala Leu Gly Leu Leu Ile Ile Gly Val Val Asn Cys Val
Ile Met Thr Gln Val Lys Lys Lys Pro Leu Cys Leu Gln Arg Glu Ala Lys Val Pro
His Leu Pro Ala Asp Lys Ala Arg Gly Thr Gln Gly Pro Glu Gln Gln His Leu Leu
Ile Thr Ala Pro Ser Ser Ser Ser Ser Ser Leu Glu Ser Ser Ala Ser Ala Leu Asp Arg
Arg Ala Pro Thr Arg Asn Gln Pro Gln Ala Pro Gly Val Glu Ala Ser Gly Ala Gly
Glu Ala Arg Ala Ser Thr Gly Ser Ser Asp Ser Ser Pro Gly Gly His Gly Thr Gln
Val Asn Val Thr Cys Ile Val Asn Val Cys Ser Ser Ser Asp His Ser Ser Gln Cys
Ser Ser Gln Ala Ser Ser Thr Met Gly Asp Thr Asp Ser Ser Pro Ser Glu Ser Pro
Lys Asp Glu Gln Val Pro Phe Ser Lys Glu Glu Cys Ala Phe Arg Ser Gln Leu Glu
Thr Pro Glu Thr Leu Leu Gly Ser Thr Glu Glu Lys Pro Leu Pro Leu Gly Val Pro
Asp Ala Gly Met Lys Pro Ser

FIG. 72A

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
Thr Ile Thr Cys Arg Ala Ser Gln Asp Val Asn Thr Ala Val Ala Trp Tyr Gln Gln
Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Phe Leu Tyr Ser Gly
Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Thr Thr Pro
Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys

FIG. 72B

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg
Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Lys Asp Thr Tyr Ile His Trp Val Arg
Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Tyr Pro Thr Asn Gly Tyr
Thr Arg Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys
Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
Tyr Cys Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr Trp Gly Gln
Gly Thr Leu Val Thr Val Ser Ser

FIG. 73A

Gln Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser Gly Met Ser Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Ala Leu Glu Trp Leu Ala Asp Ile Trp Trp Asp Asp Lys Lys Asp Tyr Asn Pro Ser Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Val Leu Lys Val Thr Asn Met Asp Pro Ala Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Ser Met Ile Thr Asn Trp Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser

FIG. 73B

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Cys Gln Leu Ser Val Gly Tyr Met His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Trp Ile Tyr Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Phe Gln Gly Ser Gly Tyr Pro Phe Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys

FIG. 74A

GACATCTTGCTGACTCAGTCTCCAGCCATCCTGTCTGTGAGTCCAGGA
GAAAGAGTCAGTTTCTCCTGCAGGGCCAGTCAGTTCGTTGGCTCAAGC
ATCCACTGGTATCAGCAAAGAACAAATGGTTCTCCAAGGCTTCTCATA
AAGTATGCTTCTGAGTCTATGTCTGGGATCCCTTCCAGGTTTAGTGGC
AGTGGATCAGGGACAGATTTTACTCTTAGCATCAACACTGTGGAGTCT
GAAGATATTGCAGATTATTACTGTCAACAAAGTCATAGCTGGCCATTC
ACGTTCGGCTCGGGGACAAATTTGGAAGTAAAAGAAGTGAAGCTTGA
GGAGTCTGGAGGAGGCTTGGTGCAACCTGGAGGATCCATGAAACTCT
CCTGTGTTGCCTCTGGATTCATTTTCAGTAACCACTGGATGAACTGGG
TCCGCCAGTCTCCAGAGAAGGGGCTTGAGTGGGTTGCTGAAATTAGA
TCAAAATCTATTAATTCTGCAACACATTATGCGGAGTCTGTGAAAGGG
AGGTTCACCATCTCAAGAGATGATTCCAAAAGTGCTGTCTACCTGCAA
ATGACCGACTTAAGAACTGAAGACACTGGCGTTTATTACTGTTCCAGG
AATTACTACGGTAGTACCTACGACTACTGGGGCCAAGGCACCACTCTC
ACAGTCTCC

FIG. 74B

Asp Ile Leu Leu Thr Gln Ser Pro Ala Ile Leu Ser Val Ser Pro Gly Glu Arg Val
Ser Phe Ser Cys Arg Ala Ser Gln Phe Val Gly Ser Ser Ile His Trp Tyr Gln Gln
Arg Thr Asn Gly Ser Pro Arg Leu Leu Ile Lys Tyr Ala Ser Glu Ser Met Ser Gly
Ile Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Ser Ile Asn
Thr Val Glu Ser Glu Asp Ile Ala Asp Tyr Tyr Cys Gln Gln Ser His Ser Trp Pro
Phe Thr Phe Gly Ser Gly Thr Asn Leu Glu Val Lys Glu Val Lys Leu Glu Glu Ser
Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Met Lys Leu Ser Cys Val Ala Ser Gly
Phe Ile Phe Ser Asn His Trp Met Asn Trp Val Arg Gln Ser Pro Glu Lys Gly Leu
Glu Trp Val Ala Glu Ile Arg Ser Lys Ser Ile Asn Ser Ala Thr His Tyr Ala Glu
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ala Val Tyr
LeuGln Met Thr Asp Leu Arg Thr Glu Asp Thr Gly Val Tyr Tyr Cys Ser Arg
Asn Tyr Tyr Gly Ser Thr Tyr Asp Tyr Trp Gly Gln Gly Thr Thr Leu Thr Val Ser

FIG. 75A

ATGGAGACAGACACACTCCTGTTATGGGTGCTGCTGCTCTGGGTTCCA
GGTTCCACTGGTGACGTCAGGCGAGGGCCCCGGAGCCTGCGGGGCAG
GGACGCGCCAGCCCCCACGCCCTGCGTCCCGGCCGAGTGCTTCGACC
TGCTGGTCCGCCACTGCGTGGCCTGCGGGCTCCTGCGCACGCCGCGGC
CGAAACCGGCCGGGGCCAGCAGCCCTGCGCCCAGGACGGCGCTGCAG
CCGCAGGAGTCGGTGGGCGCGGGGGCCGGCGAGGCGGCGGTCGACA
AAACTCACACATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGA
CCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATC
TCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGA
AGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGC
ATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTA
CCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGG
CAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCA
TCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAG
GTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGT
CAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGT
GGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACG
CCTCCCGTGTTGGACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTC
ACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTC
CGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCT
CCCTGTCTCCCGGGAAATGA

FIG. 75B

Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro Gly Ser
Thr Gly Asp Val Arg Arg Gly Pro Arg Ser Leu Arg Gly Arg Asp Ala Pro Ala
Pro Thr Pro Cys Val Pro Ala Glu Cys Phe Asp Leu Leu Val Arg His Cys Val Ala
Cys Gly Leu Leu Arg Thr Pro Arg Pro Lys Pro Ala Gly Ala Ser Ser Pro Ala Pro
Arg Thr Ala Leu Gln Pro Gln Glu Ser Val Gly Ala Gly Ala Gly Glu Ala Ala Val
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys

FIG. 76

Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly Asp Arg Val
Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Asn Asn Tyr Leu Asn Trp Tyr Gln Gln
Lys Pro Asp Gly Ile Val Lys Leu Leu Ile Tyr Tyr Thr Ser Thr Leu His Ser Gly
Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser
Asn Leu Glu Gln Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro
Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys

FIG. 77

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Gly Pro Gly Thr Ser Val Arg Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Leu Ile Glu Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Thr Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Asp Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ala

FIG. 78

Asp Ile Gln Met Thr Gln Thr Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val
Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Asn Asn Tyr Leu Asn Trp Tyr Gln Gln
Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser Thr Leu His Ser Gly
Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser
Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu
Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Val Lys

FIG. 79

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Leu Ile Glu Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe Lys Gly Arg Val Thr Leu Thr Val Asp Glu Ser Thr Asn Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser

FIG. 80

Asp Ile Gln Met Thr Gln Thr Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val
Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Asn Asn Tyr Leu Asn Trp Tyr Gln Gln
Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser Thr Leu His Ser Gly
Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser
Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu
Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Val Lys Arg Thr Val Ala Ala Pro
Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val
Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys
Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
Ser Phe Asn Arg Gly Glu Cys

FIG. 81

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser Ser Val Lys
Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Leu Ile Glu Trp Val Arg
Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Val Ile Tyr Pro Gly Ser Gly Gly
Thr Asn Tyr Asn Glu Lys Phe Lys Gly Arg Val Thr Leu Thr Val Asp Glu Ser
Thr Asn Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr
Phe Cys Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Gln Gly
Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe
Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp
Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly

FIG. 82A

ATGGATTTTCAGGTGCAGATTATCAGCTTCCTGCTAATCAGTGCTTCA
GTCATAATGTCCAGAGGGCAAATTGTTCTCTCCCAGTCTCCAGCAATC
CTGTCTGCATCTCCAGGGGAGAAGGTCACAATGACTTGCAGGGCCAG
CTCAAGTGTAAGTTACATCCACTGGTTCCAGCAGAAGCCAGGATCCTC
CCCCAAACCCTGGATTTATGCCACATCCAACCTGGCTTCTGGAGTCCC
TGTTCGCTTCAGTGGCAGTGGGTCTGGGACTTCTTACTCTCTCACAAT
CAGCAGAGTGGAGGCTGAAGATGCTGCCACTTATTACTGCCAGCAGT
GGACTAGTAACCCACCCACGTTCGGAGGGGGGACCAAGCTGGAAATC
AAA

FIG. 82B

Met Asp Phe Gln Val Gln Ile Ile Ser Phe Leu Leu Ile Ser Ala Ser Val Ile Met Ser
Arg Gly Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly Glu
Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Ile His Trp Phe Gln
Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr Ala Thr Ser Asn Leu Ala Ser
Gly Val Pro Val Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile
Ser Arg Val Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Ser Asn
Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys

FIG. 83A

ATGGGTTGGAGCCTCATCTTGCTCTTCCTTGTCGCTGTTGCTACGCGTG
TCCTGTCCCAGGTACAACTGCAGCAGCCTGGGGCTGAGCTGGTGAAG
CCTGGGGCCTCAGTGAAGATGTCCTGCAAGGCTTCTGGCTACACATTT
ACCAGTTACAATATGCACTGGGTAAAACAGACACCTGGTCGGGGCCT
GGAATGGATTGGAGCTATTTATCCCGGAAATGGTGATACTTCCTACAA
TCAGAAGTTCAAAGGCAAGGCCACATTGACTGCAGACAAATCCTCCA
GCACAGCCTACATGCAGCTCAGCAGCCTGACATCTGAGGACTCTGCG
GTCTATTACTGTGCAAGATCGACTTACTACGGCGGTGACTGGTACTTC
AATGTCTGGGGCGCAGGGACCACGGTCACCGTCTCTGCA

FIG. 83B

Met Gly Trp Ser Leu Ile Leu Leu Phe Leu Val Ala Val Ala Thr Arg Val Leu Ser
Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys
Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asn Met His Trp Val Lys
Gln Thr Pro Gly Arg Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn Gly Asp
Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser
Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr
Cys Ala Arg Ser Thr Tyr Tyr Gly Gly Asp Trp Tyr Phe Asn Val Trp Gly Ala Gly
Thr Thr Val Thr Val Ser Ala

FIG. 84A

CAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTG
ACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAG
AGCTGGGTACGTCCTCACATTCAGTGATCAGCACTGAACACAGACCC
GTCGACATGGGTTGGAGCCTCATCTTGCTCTTCCTTGTCGCTGTTGCTA
CGCGTGTCGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCT
CCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTC
AAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGC
CCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGG
ACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGG
CACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCA
AGGTGGACAAGAAAGCAGAGCCCAAATCTTGTGACAAAACTCACACA
TGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTTC
CTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCT
GAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGT
CAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGA
CAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGC
GTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGACTACAA
GTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCA
TCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTG
CCCCCATCCCGGGATGAGCTGACCAGGAACCAGGTCAGCCTGACCTG
CCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGA
GCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTG
GACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAG
AGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGA
GGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGG
TAAATGAGGATCCGTTAACGGTTACCAACTACCTAGACTGGATTCGTG
ACAACATGCGGCCGTGATATCTACGTATGATCAGCCTCGACTGTGCCT
TCTAGTTGCCAGCCATCTGTTGTTTGCCCCTCCCCCGTGCCTTCCTTGA
CCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGGAAA
TTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGGG
TGGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGCA
TGCTGGGGATGCGGTGGGCTCTATGGAACCAGCTGGGGCTCGACAGC
GCTGGATCTCCCGATCCCCAGCTTTGCTTCTCAATTTCTTATTTGCATA
ATGAGAAAAAAAGGAAAATTAATTTTAACACCAATTCAGTAGTTGAT
TGAGCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACAGTGTTCTCT
GCACAGATAAGGACAAACATTATTCAGAGGGAGTACCCAGAGCTGAG
ACTCCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGAAATATGCTT
GTCATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGGTAAGGGCC
AATCTGCTCACACAGGATAGAGAGGGCAGGAGCCAGGGCAGAGCAT
ATAAGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTCTGACATAG
TTGTGTTGGGAGCTTGGATAGCTTGGACAGCTCAGG

FIG. 84B

CAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTG
ACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAG
AGCTGGGTACGTCCTCACATTCAGTGATCAGCACTGAACACAGACCC
GTCGACATGGGTTGGAGCCTCATCTTGCTCTTCCTTGTCGCTGTTGCTA
CGCGTGTCGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCT
CCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTC
AAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGC
CCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGG
ACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGG
CACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCA
AGGTGGACAAGAAAGCAGAGCCCAAATCTTGTGACAAAACTCACACA
TGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTTC
CTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCT
GAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGT
CAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGA
CAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGC
GTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGACTACAA
GTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCA
TCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTG
CCCCCATCCCGGGATGAGCTGACCAGGAACCAGGTCAGCCTGACCTG
CCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGA
GCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTG
GACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAG
AGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGA
GGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGG
TAAATGAGGATCCGTTAACGGTTACCAACTACCTAGACTGGATTCGTG
ACAACATGCGGCCGTGATATCTACGTATGATCAGCCTCGACTGTGCCT
TCTAGTTGCCAGCCATCTGTTGTTTGCCCCTCCCCCGTGCCTTCCTTGA
CCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGGAAA
TTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGGG
TGGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGCA
TGCTGGGGATGCGGTGGGCTCTATGGAACCAGCTGGGGCTCGACAGC
GCTGGATCTCCCGATCCCCAGCTTTGCTTCTCAATTTCTTATTTGCATA
ATGAGAAAAAAAGGAAAATTAATTTTAACACCAATTCAGTAGTTGAT
TGAGCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACAGTGTTCTCT
GCACAGATAAGGACAAACATTATTCAGAGGGAGTACCCAGAGCTGAG
ACTCCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGAAATATGCTT
GTCATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGGTAAGGGCC
AATCTGCTCACACAGGATAGAGAGGGCAGGAGCCAGGGCAGAGCAT
ATAAGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTCTGACATAG
TTGTGTTGGGAGCTTGGATAGCTTGGACAGCTCAGG

FIG. 84C

GCTGCGATTTCGCGCCAAACTTGACGGCAATCCTAGCGTGAAGGCTG
GTAGGATTTTATCCCCGCTGCCATCATGGTTCGACCATTGAACTGCAT
CGTCGCCGTGTCCCAAAATATGGGGATTGGCAAGAACGGAGACCTAC
CCTGGCCTCCGCTCAGGAACGAGTTCAAGTACTTCCAAAGAATGACC
ACAACCTCTTCAGTGGAAGGTAAACAGAATCTGGTGATTATGGGTAG
GAAAACCTGGTTCTCCATTCCTGAGAACAATCGACCTTTAAAGGACA
GAATTAATATAGTTCTCAGTAGAGAACTCAAAGAACCACCACGAGGA
GCTCATTTTCTTGCCAAAAGTTTGGATGATGCCTTAAGACTTATTGAA
CAACCGGAATTGGCAAGTAAAGTAGACATGGTTTGGATAGTCGGAGG
CAGTTCTGTTTACCAGGAAGCCATGAATCAACCAGGCCACCTTAGACT
CTTTGTGACAAGGATCATGCAGGAATTTGAAAGTGACACGTTTTTCCC
AGAAATTGATTTGGGGAAATATAAACTTCTCCCAGAATACCCAGGCG
TCCTCTCTGAGGTCCAGGAGGAAAAAGGCATCAAGTATAAGTTTGAA
GTCTACGAGAAGAAAGACTAACAGGAAGATGCTTTCAAGTTCTCTGC
TCCCCTCCTAAAGTCATGCATTTTTATAAGACCATGGGACTTTTGCTG
GCTTTAGATCAGCCTCGACTGTGCCTTCTAGTTGCCAGCCATCTGTTGT
TTGCCCCTCCCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCAC
TGTCCTTTCCTAATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAG
GTGTCATTCTATTCTGGGGGGTGGGGTGGGGCAGGACAGCAAGGGGG
AGGATTGGGAAGACAATAGCAGGCATGCTGGGGATGCGGTGGGCTCT
ATGGAACCAGCTGGGGCTCGAGCTACTAGCTTTGCTTCTCAATTTCTT
ATTTGCATAATGAGAAAAAAAGGAAAATTAATTTTAACACCAATTCA
GTAGTTGATTGAGCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACA
GTGTTCTCTGCACAGATAAGGACAAACATTATTCAGAGGGAGTACCC
AGAGCTGAGACTCCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGA
AATATGCTTGTCATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGG
TAAGGGCCAATCTGCTCACACAGGATAGAGAGGGCAGGAGCCAGGG
CAGAGCATATAAGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTC
TGACATAGTTGTGTTGGGAGCTTGGATCGATCCTCTATGGTTGAACAA
GATGGATTGCACGCAGGTTCTCCGGCCGCTTGGGTGGAGAGGCTATTC
GGCTATGACTGGGCACAACAGACAATCGGCTGCTCTGATGCCGCCGT
GTTCCGGCTGTCAGCGCAGGGGCGCCCGGTTCTTTTTGTCAAGACCGA
CCTGTCCGGTGCCCTGAATGAACTGCAGGACGAGGCAGCGCGGCTAT
CGTGGCTGGCCACGACGGGCGTTCCTTGCGCAGCTGTGCTCGACGTTG
TCACTGAAGCGGGAAGGGACTGGCTGCTATTGGGCGAAGTGCCGGGG
CAGGATCTCCTGTCATCTCACCTTGCTCCTGCCGAGAAAGTATCCATC
ATGGCTGATGCAATGCGGCGGCTGCATACGCTTGATCCGGCTACCTGC
CCATTCGACCACCAAGCGAAACATCGCATCGAGCGAGCACGTACTCG
GATGGAAGCCGGTCTTGTCGATCAGGATGATCTGGACGAAGAGCATC
AGGGGCTCGCGCCAGCCGAACTGTTCGCCAGGCTCAAGGCGCGCATG
CCCGACGGCGAGGATCTCGTCGTGACCCATGGCGATGCCTGCTTGCCG

FIG. 84D

AATATCATGGTGGAAAATGGCCGCTTTTCTGGATTCATCGACTGTGGC
CGGCTGGGTGTGGCGGACCGCTATCAGGACATAGCGTTGGCTACCCG
TGATATTGCTGAAGAGCTTGGCGGCGAATGGGCTGACCGCTTCCTCGT
GCTTTACGGTATCGCCGCTTCCCGATTCGCAGCGCATCGCCTTCTATC
GCCTTCTTGACGAGTTCTTCTGAGCGGGACTCTGGGGTTCGAAATGAC
CGACCAAGCGACGCCCAACCTGCCATCACGAGATTTCGATTCCACCG
CCGCCTTCTATGAAAGGTTGGGCTTCGGAATCGTTTTCCGGGACGCCG
GCTGGATGATCCTCCAGCGCGGGGATCTCATGCTGGAGTTCTTCGCCC
ACCCCAACTTGTTTATTGCAGCTTATAATGGTTACAAATAAAGCAATA
GCATCACAAATTTCACAAATAAAGCATTTTTTTCACTGCATTCTAGTT
GTGGTTTGTCCAAACTCATCAATCTATCTTATCATGTCTGGATCGCGG
CCGCGATCCCGTCGAGAGCTTGGCGTAATCATGGTCATAGCTGTTTCC
TGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCGG
AGCATAAAGTGTAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCAC
ATTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTC
GTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTT
TGCGTATTGGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTC
GGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAA
TACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGA
GCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGC
TGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATC
GACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATAC
CAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACC
CTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTG
GCGCTTTCTCAATGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTC
GTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGAC
CGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGA
CACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAG
AGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTA
ACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGA
AGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAA
CAAACCACCGCTGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATT
ACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTAC
GGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGG
TCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAA
AATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTG
ACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTC
TATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTAC
GATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGC
GAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCA
GCCGGAAGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTC
CATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGC

FIG. 84E

CAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGG
TGTCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAAC
GATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGGTT
AGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTG
TTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGC
CATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCAT
TCTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAA
TACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATC
ATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGCTG
TTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCA
GCATCTTTTACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGG
CAAAATGCCGCAAAAAAGGGAATAAGGGCGACACGGAAATGTTGAA
TACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCAGGGTTA
TTGTCTCATGAGCGGATACATATTTGAATGTATTTAGAAAAATAAACA
AATAGGGGTTCCGCGCACATTTCCCCGAAAAGTGCCACCT

FIG. 85A

GACGTCGCGGCCGCTCTAGGCCTCCAAAAAAGCCTCCTCACTACTTCT
GGAATAGCTCAGAGGCCGAGGCGGCCTCGGCCTCTGCATAAATAAAA
AAAATTAGTCAGCCATGCATGGGGCGGAGAATGGGCGGAACTGGGCG
GAGTTAGGGGCGGGATGGGCGGAGTTAGGGGCGGGACTATGGTTGCT
GACTAATTGAGATGCATGCTTTGCATACTTCTGCCTGCTGGGGAGCCT
GGGGACTTTCCACACCTGGTTGCTGACTAATTGAGATGCATGCTTTGC
ATACTTCTGCCTGCTGGGGAGCCTGGGGACTTTCCACACCCTAACTGA
CACACATTCCACAGAATTAATTCCCCTAGTTATTAATAGTAATCAATT
ACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAA
CTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCC
ATTGACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGGA
CTTTCCATTGACGTCAATGGGTGGACTATTTACGGTAAACTGCCCACT
TGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACG
TCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCT
TATGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTA
TTACCATGGTGATGCGGTTTTGGCAGTACATCAATGGGCGTGGATACC
GGTTTGACTCACGCGGATTTCCAAGTCTCCACCCCATTGACGTCAATG
GGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTA
ACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGG
GAGGTCTATATAAGCAGAGCTGGGTACGTGAACCGTCAGATCGCCTG
GAGACGCCATCACAGATCTCTCACTATGGATTTTCAGGTGCAGATTAT
CAGCTTCCTGCTAATCAGTGCTTCAGTCATAATGTCCAGAGGACAAAT
TGTTCTCTCCCAGTCTCCAGCAATCCTGTCTGCATCTCCAGGGGAGAA
GGTCACAATGACTTGCAGGGCCAGCTCAAGTGTAAGTTACATCCACT
GGTTCCAGCAGAAGCCAGGATCCTCCCCCAAACCCTGGATTTATGCCA
CATCCAACCTGGCTTCTGGAGTCCCTGTTCGCTTCAGTGGCAGTGGGT
CTGGGACTTCTTACTCTCTCACAATCAGCAGAGTGGAGGCTGAAGATG
CTGCCACTTATTACTGCCAGCAGTGGACTAGTAACCCACCCACGTTCG
GAGGGGGGACCAAGCTGGAAATCAAACGTACGGTGGCTGCACCATCT
GTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGCC
TCTGTTGTGTGCCTGCTGAATAACTTCTATCCCAGAGAGGCCAAAGTA
CAGTGGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCCAGGAGAG
TGTCACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAGCAGCA
CCCTGACGCTGAGCAAAGCAGACTACGAGAAACACAAAGTCTACGCC
TGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTT
CAACAGGGGAGAGTGTTGAATTCAGATCCGTTAACGGTTACCAACTA
CCTAGACTGGATTCGTGACAACATGCGGCCGTGATATCTACGTATGAT
CAGCCTCGACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGCCCCTC
CCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCC

FIG. 85B

TAATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCT
ATTCTGGGGGGTGGGGTGGGGCAGGACAGCAAGGGGGAGGATTGGG
AAGACAATAGCAGGCATGCTGGGGATGCGGTGGGCTCTATGGAACCA
GCTGGGGCTCGACAGCTATGCCAAGTACGCCCCCTATTGACGTCAATG
ACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGG
ACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCAT
GGTGATGCGGTTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTG
ACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGGAGTT
TGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACT
CCGCCCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTC
TATATAAGCAGAGCTGGGTACGTCCTCACATTCAGTGATCAGCACTGA
ACACAGACCCGTCGACATGGGTTGGAGCCTCATCTTGCTCTTCCTTGT
CGCTGTTGCTACGCGTGTCCTGTCCCAGGTACAACTGCAGCAGCCTGG
GGCTGAGCTGGTGAAGCCTGGGGCCTCAGTGAAGATGTCCTGCAAGG
CTTCTGGCTACACATTTACCAGTTACAATATGCACTGGGTAAAACAGA
CACCTGGTCGGGGCCTGGAATGGATTGGAGCTATTTATCCCGGAAAT
GGTGATACTTCCTACAATCAGAAGTTCAAAGGCAAGGCCACATTGAC
TGCAGACAAATCCTCCAGCACAGCCTACATGCAGCTCAGCAGCCTGA
CATCTGAGGACTCTGCGGTCTATTACTGTGCAAGATCGACTTACTACG
GCGGTGACTGGTACTTCAATGTCTGGGGCGCAGGGACCACGGTCACC
GTCTCTGCAGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCC
TCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGT
CAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCG
CCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAG
GACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGG
GCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACC
AAGGTGGACAAGAAAGCAGAGCCCAAATCTTGTGACAAAACTCACAC
ATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTT
CCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCC
TGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGG
TCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAG
ACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAG
CGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACA
AGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACC
ATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCT
GCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCT
GCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAG
AGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCT
GGACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAA
GAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATG
AGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGG
GTAAATGAGGATCCGTTAACGGTTACCAACTACCTAGACTGGATTCGT

FIG. 85C

```
GACAACATGCGGCCGTGATATCTACGTATGATCAGCCTCGACTGTGCC
TTCTAGTTGCCAGCCATCTGTTGTTTGCCCCTCCCCCGTGCCTTCCTTG
ACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGGAA
ATTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGG
GTGGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGC
ATGCTGGGGATGCGGTGGGCTCTATGGAACCAGCTGGGGCTCGACAG
CGCTGGATCTCCCGATCCCCAGCTTTGCTTCTCAATTTCTTATTTGCAT
AATGAGAAAAAAAGGAAAATTAATTTTAACACCAATTCAGTAGTTGA
TTGAGCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACAGTGTTCTCT
GCACAGATAAGGACAAACATTATTCAGAGGGAGTACCCAGAGCTGAG
ACTCCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGAAATATGCTT
GTCATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGGTAAGGGCC
AATCTGCTCACACAGGATAGAGAGGGCAGGAGCCAGGGCAGAGCAT
ATAAGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTCTGACATAG
TTGTGTTGGGAGCTTGGATAGCTTGGACAGCTCAGGGCTGCGATTTCG
CGCCAAACTTGACGGCAATCCTAGCGTGAAGGCTGGTAGGATTTTATC
CCCGCTGCCATCATGGTTCGACCATTGAACTGCATCGTCGCCGTGTCC
CAAAATATGGGGATTGGCAAGAACGGAGACCTACCCTGGCCTCCGCT
CAGGAACGAGTTCAAGTACTTCCAAAGAATGACCACAACCTCTTCAG
TGGAAGGTAAACAGAATCTGGTGATTATGGGTAGGAAAACCTGGTTC
TCCATTCCTGAGAAGAATCGACCTTTAAAGGACAGAATTAATATAGTT
CTCAGTAGAGAACTCAAAGAACCACCACGAGGAGCTCATTTTCTTGC
CAAAAGTTTGGATGATGCCTTAAGACTTATTGAACAACCGGAATTGG
CAAGTAAAGTAGACATGGTTTGGATAGTCGGAGGCAGTTCTGTTTACC
AGGAAGCCATGAATCAACCAGGCCACCTTAGACTCTTTGTGACAAGG
ATCATGCAGGAATTTGAAAGTGACACGTTTTTCCCAGAAATTGATTTG
GGGAAATATAAACTTCTCCCAGAATACCCAGGCGTCCTCTCTGA
GGTCCAGGAGGAAAAAGGCATCAAGTATAAGTTTGAAGTCTACGAGA
AGAAAGACTAACAGGAAGATGCTTTCAAGTTCTCTGCTCCCCTCCTAA
AGCTATGCATTTTTATAAGACCATGGACTTTTGCTGGCTTTAGATCA
GCCTCGACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGCCCCTCCC
CCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTA
ATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCTAT
TCTGGGGGGTGGGGTGGGGCAGGACAGCAAGGGGGAGGATTGGGAA
GACAATAGCAGGCATGCTGGGGATGCGGTGGGCTCTATGGAACCAGC
TGGGGCTCGAGCTACTAGCTTTGCTTCTCAATTTCTTATTTGCATAATG
AGAAAAAAAGGAAAATTAATTTTAACACCAATTCAGTAGTTGATTGA
GCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACAGTGTTCTCTGCA
CAGATAAGGACAAACATTATTCAGAGGGAGTACCCAGAGCTGAGACT
CCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGAAATATGCTTGTC
ATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGGTAAGGGCCAAT
CTGCTCACACAGGATAGAGAGGGCAGGAGCCAGGGCAGAGCATATA
AGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTCTGACATAGTTG
```

FIG. 85D

TGTTGGGAGCTTGGATCGATCCTCTATGGTTGAACAAGATGGATTGCA
CGCAGGTTCTCCGGCCGCTTGGGTGGAGAGGCTATTCGGCTATGACTG
GGCACAACAGACAATCGGCTGCTCTGATGCCGCCGTGTTCCGGCTGTC
AGCGCAGGGGCGCCCGGTTCTTTTTGTCAAGACCGACCTGTCCGGTGC
CCTGAATGAACTGCAGGACGAGGCAGCGCGGCTATCGTGGCTGGCCA
CGACGGGCGTTCCTTGCGCAGCTGTGCTCGACGTTGTCACTGAAGCGG
GAAGGGACTGGCTGCTATTGGGCGAAGTGCCGGGGCAGGATCTCCTG
TCATCTCACCTTGCTCCTGCCGAGAAAGTATCCATCATGGCTGATGCA
ATGCGGCGGCTGCATACGCTTGATCCGGCTACCTGCCCATTCGACCAC
CAAGCGAAACATCGCATCGAGCGAGCACGTACTCGGATGGAAGCCGG
TCTTGTCGATCAGGATGATCTGGACGAAGAGCATCAGGGGCTCGCGC
CAGCCGAACTGTTCGCCAGGCTCAAGGCGCGCATGCCCGACGGCGAG
GATCTCGTCGTGACCCATGGCGATGCCTGCTTGCCGAATATCATGGTG
GAAAATGGCCGCTTTTCTGGATTCATCGACTGTGGCCGGCTGGGTGTG
GCGGACCGCTATCAGGACATAGCGTTGGCTACCCGTGATATTGCTGA
AGAGCTTGGCGGCGAATGGGCTGACCGCTTCCTCGTGCTTTACGGTAT
CGCCGCTCCCGATTCGCAGCGCATCGCCTTCTATCGCCTTCTTGACGA
GTTCTTCTGAGCGGGACTCTGGGGTTCGAAATGACCGACCAAGCGAC
GCCCAACCTGCCATCACGAGATTTCGATTCCACCGCCGCCTTCTATGA
AAGGTTGGGCTTCGGAATCGTTTTCCGGGACGCCGGCTGGATGATCCT
CCAGCGCGGGGATCTCATGCTGGAGTTCTTCGCCCACCCCAACTTGTT
TATTGCAGCTTATAATGGTTACAAATAAAGCAATAGCATCACAAATTT
CACAAATAAAGCATTTTTTTCACTGCATTCTAGTTGTGGTTTGTCCAA
ACTCATCAATCTATCTTATCATGTCTGGATCGCGGCCGCGATCCCGTC
GAGAGCTTGGCGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGT
TATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCATAAAGTG
TAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTT
GCGCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTCGTGCCAGCTGCA
TTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGGC
GCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCT
GCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCA
CAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCA
GCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCC
ATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGT
CAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCC
CCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTAC
CGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCA
ATGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAA
GCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTT
ATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATC

FIG. 53A

GCGCCTCTTATGTACCCACAAAAATCTATTTTCAAAAAAGTTGCTCTA
AGAATATAGTTATCAAGTTAAGTAAAATGTCAATAGCCTTTTAATTTA
ATTTTTAATTGTTTTATCATTCTTTGCAATAATAAAACATTAACTTTAT
ACTTTTTAATTTAATGTATAGAATAGAGATATACATAGGATATGTAAA
TAGATACACAGTGTATATGTGATTAAAATATAATGGGAGATTCAATC
AGAAAAAAGTTTCTAAAAAGGCTCTGGGGTAAAAGAGGAAGGAAAC
AATAATGAAAAAAATGTGGTGAGAAAAACAGCTGAAAACCCATGTA
AAGAGTGTATAAAGAAAGCAAAAAGAGAAGTAGAAAGTAACACAGG
GGCATTTGGAAAATGTAAACGAGTATGTTCCCTATTTAAGGCTAGGC
ACAAAGCAAGGTCTTCAGAGAACCTGGAGCCTAAGGTTTAGGCTCAC
CCATTTCAACCAGTCTAGCAGCATCTGCAACATCTACAATGGCCTTGA
CCTTTGCTTTACTGGTGGCCCTCCTGGTGCTCAGCTGCAAGTCAAGCT
GCTCTGTGGGCTGTGATCTGCCTCAAACCCACAGCCTGGGTAGCAGG
AGGACCTTGATGCTCCTGGCACAGATGAGGAGAATCTCTCTTTTCTCC
TGCTTGAAGGACAGACATGACTTTGGATTTCCCCAGGAGGAGTTTGG
CAACCAGTTCCAAAAGGCTGAAACCATCCCTGTCCTCCATGAGATGA
TCCAGCAGATCTTCAATCTCTTCAGCACAAAGGACTCATCTGCTGCTT
GGGATGAGACCCTCCTAGACAAATTCTACACTGAACTCTACCAGCAG
CTGAATGACCTGGAAGCCTGTGTGATACAGGGGGTGGGGGTGACAGA
GACTCCCCTGATGAAGGAGGACTCCATTCTGGCTGTGAGGAAATACT
TCCAAAGAATCACTCTCTATCTGAAAGAGAAGAAATACAGCCCTTGT
GCCTGGGAGGTTGTCAGAGCAGAAATCATGAGATCTTTTTCTTTGTCA
ACAAACTTGCAAGAAAGTTTAAGAAGTAAGGAATGAAAACTGGTTCA
ACATGGAAATGATTTTCATTGATTCGTATGCCAGCTCACCTTTTTATG
ATCTGCCATTTCAAAGACTCATGTTTCTGCTATGACCATGACACGATT
TAAATCTTTTCAAATGTTTTTAGGAGTATTAATCAACATTGTATTCAG
CTCTTAAGGCACTAGTCCCTTACAGAGGACCATGCTGACTGATCCATT
ATCTATTTAAATATTTTTAAAATATTATTTATTTAACTATTTATAAAAC
AACTTATTTTTGTTCATATTATGTCATGTGCACCTTTGCACAGTGGTTA
ATGTAATAAAATGTGTTCTTTGTATTTGGTAAATTTATTTTGTGTTGTT
CATTGAACTTTTGCTATGGAACTTTTGTACTTGTTTATTCTTTAAAATG
AAATTCCAAGCCTAATTGTGCAACCTGATTACAGAATAACTGGTACA
CTTCATTTGTCCATCAATATTATATTCAAGATATAAGTAAAAATAAAC
TTTCTGTAAACCAAGTTGTATGTTGTACTCAAGATAACAGGGTGAACC
TAACAAATACAATTCTGCTCTCTTGTGTATTTGATTTTTGTATGAAAA
AAACTAAAAATGGTAATCATACTTAATTATCAGTTATGGTAAATGGT
ATGAAGAGAAGAAGGAACG

FIG. 85E

GCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATG
TAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTAC
ACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACC
TTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGC
TGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAA
AAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGC
TCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATC
AAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAA
ATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATG
CTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCC
ATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGG
CTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTC
ACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCG
AGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTATTA
ATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGC
GCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGT
TTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTA
CATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTC
CGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTA
TGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGATGCT
TTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTA
TGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAATACGGGATAATACC
GCGCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCT
TCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCG
ATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCA
CCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAA
AAGGGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCT
TTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGG
ATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTTCCGC
GCACATTTCCCCGAAAAGTGCCACCT

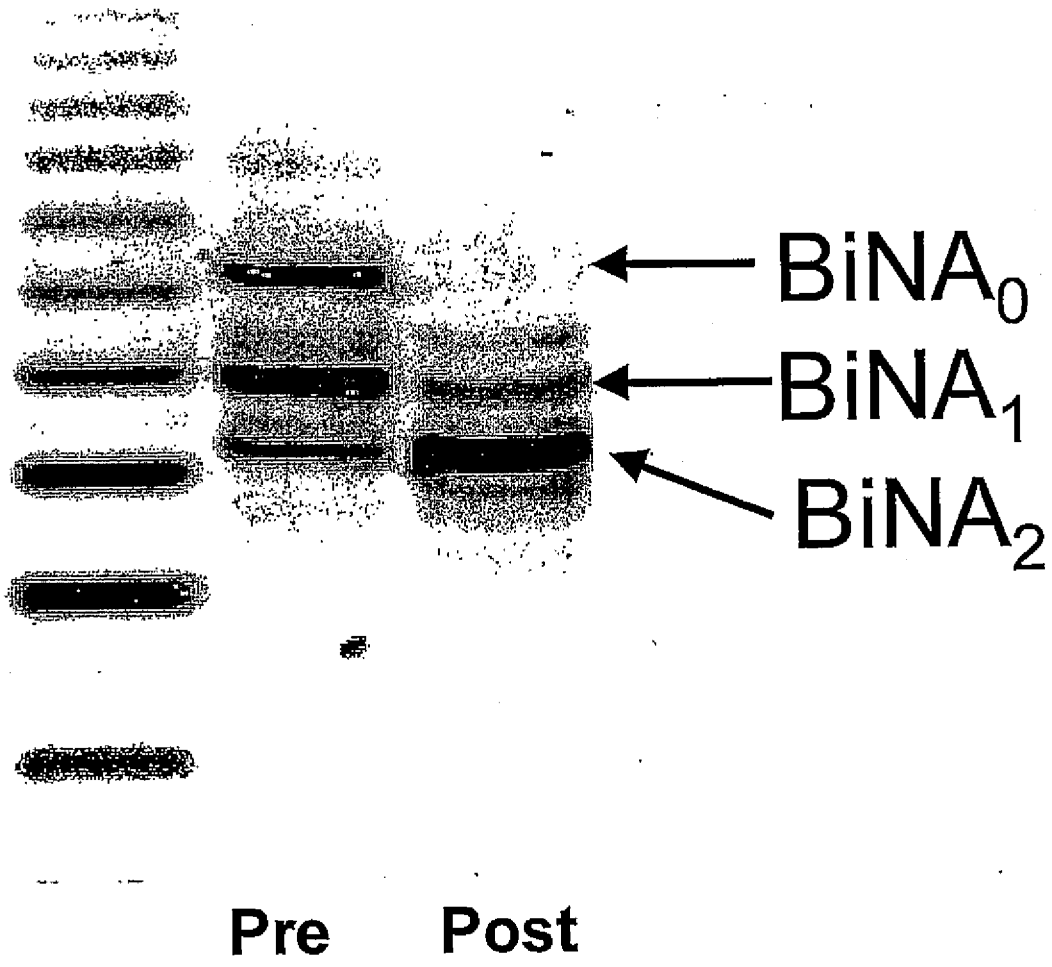


FIG. 86

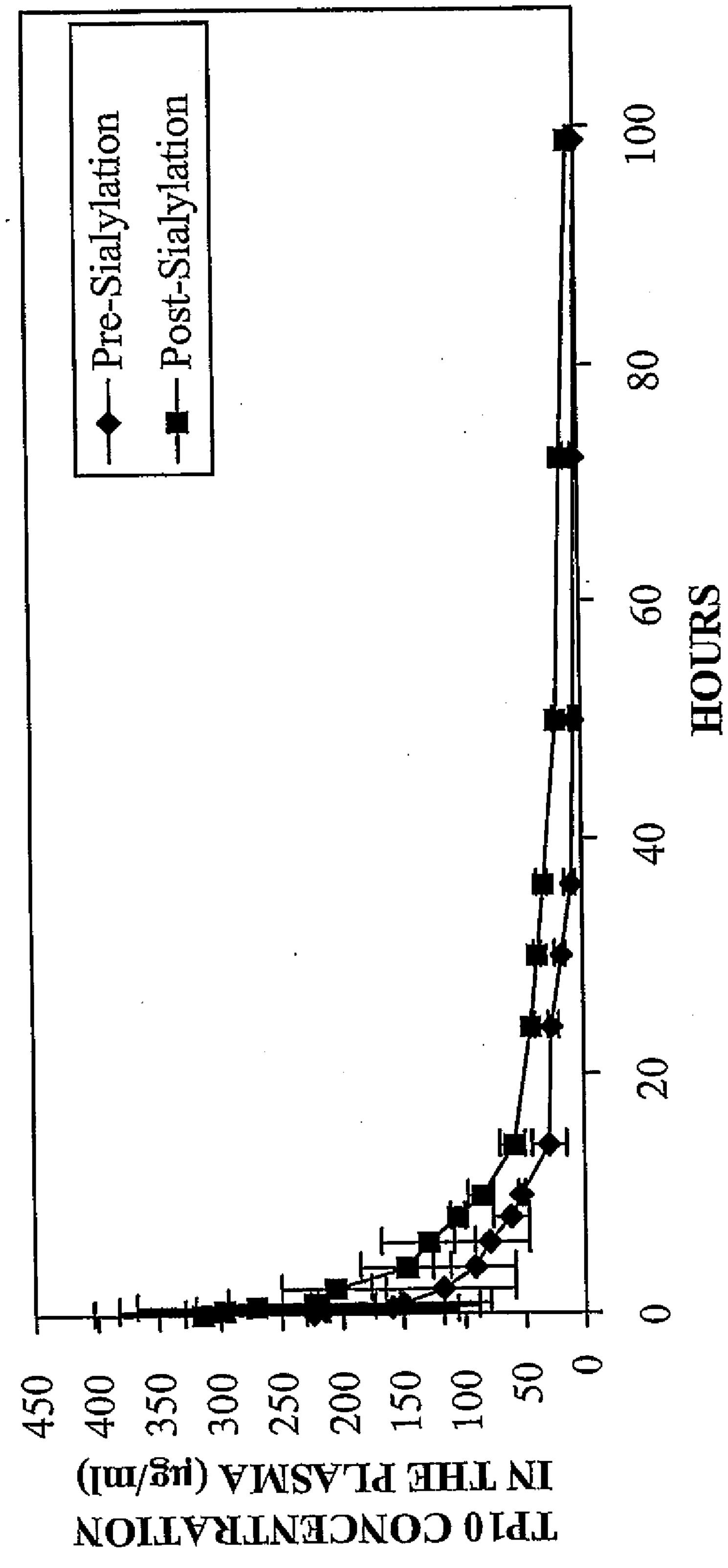

Pre-Sialylation
Post-Sialylation
TP10 CONCENTRATION IN THE PLASMA (μg/ml)
450
400
350
300
250
200
150
100
50
0
HOURS
0
20
40
60
80
100

FIG. 87

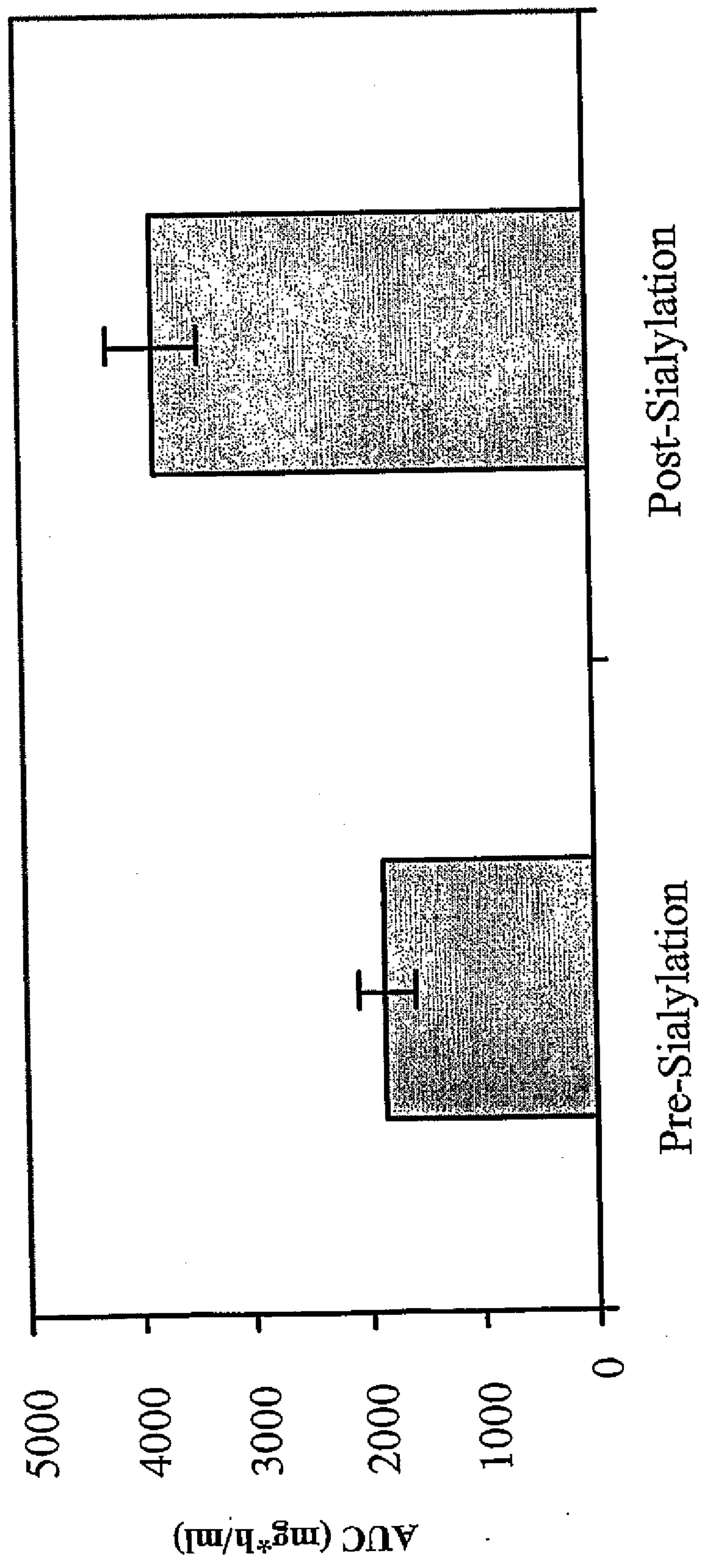

AUC (mg*h/ml)
5000
4000
3000
2000
1000
0
Pre-Sialylation
Post-Sialylation

FIG. 88

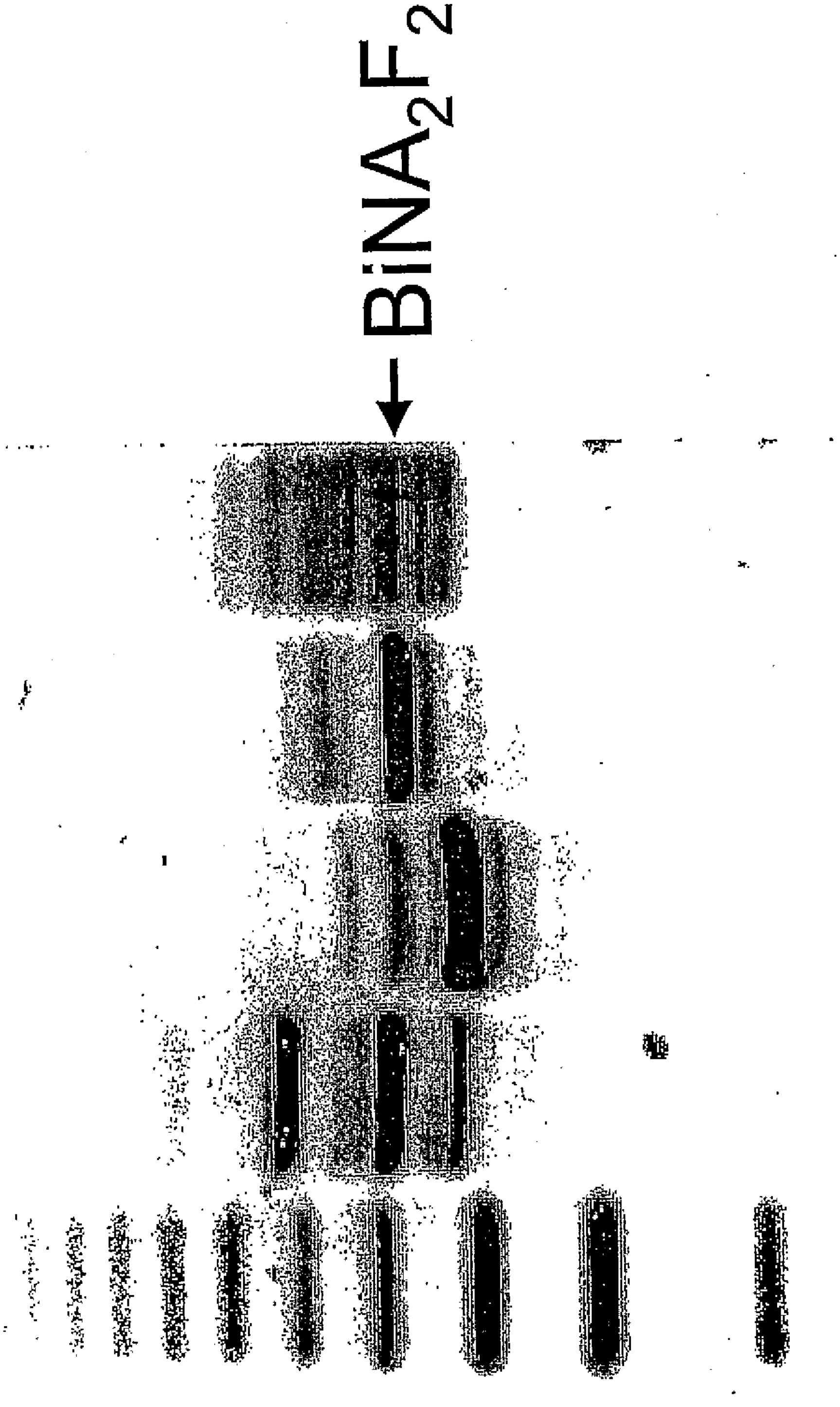


FIG. 89

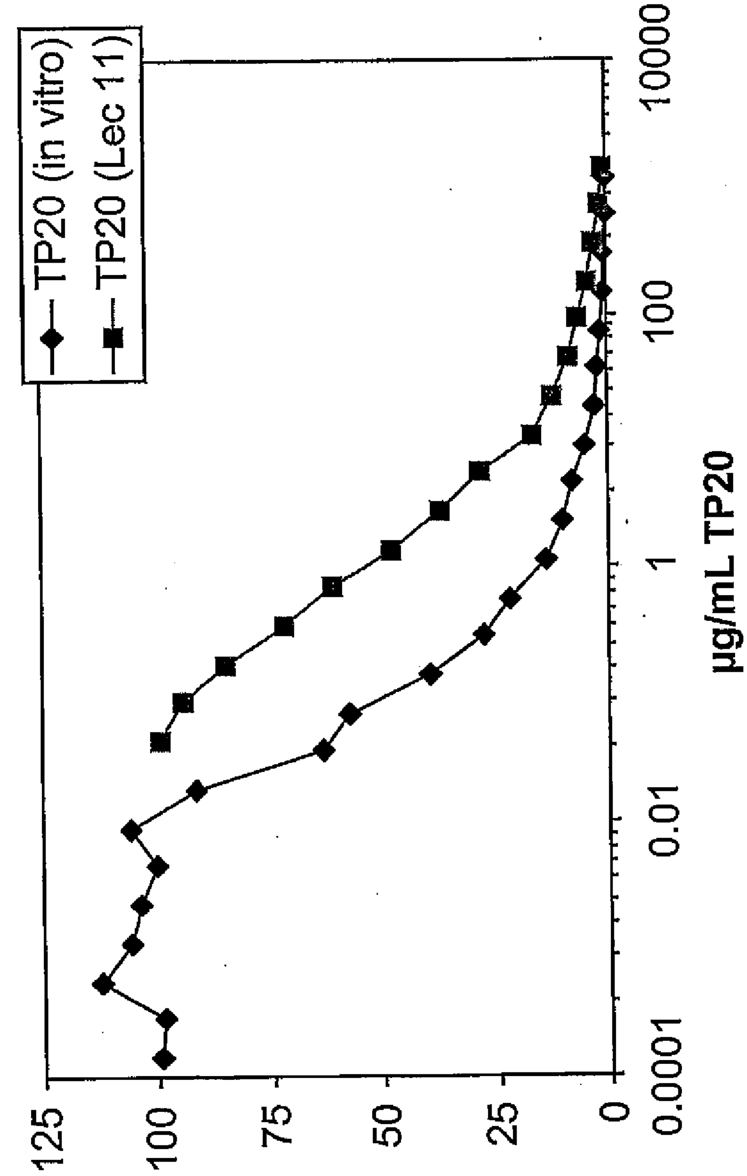

TP20 (in vitro)
TP20 (Lec 11)
125
100
75
50
25
0
0.0001
0.01
1
100
10000
µg/mL TP20

FIG. 90

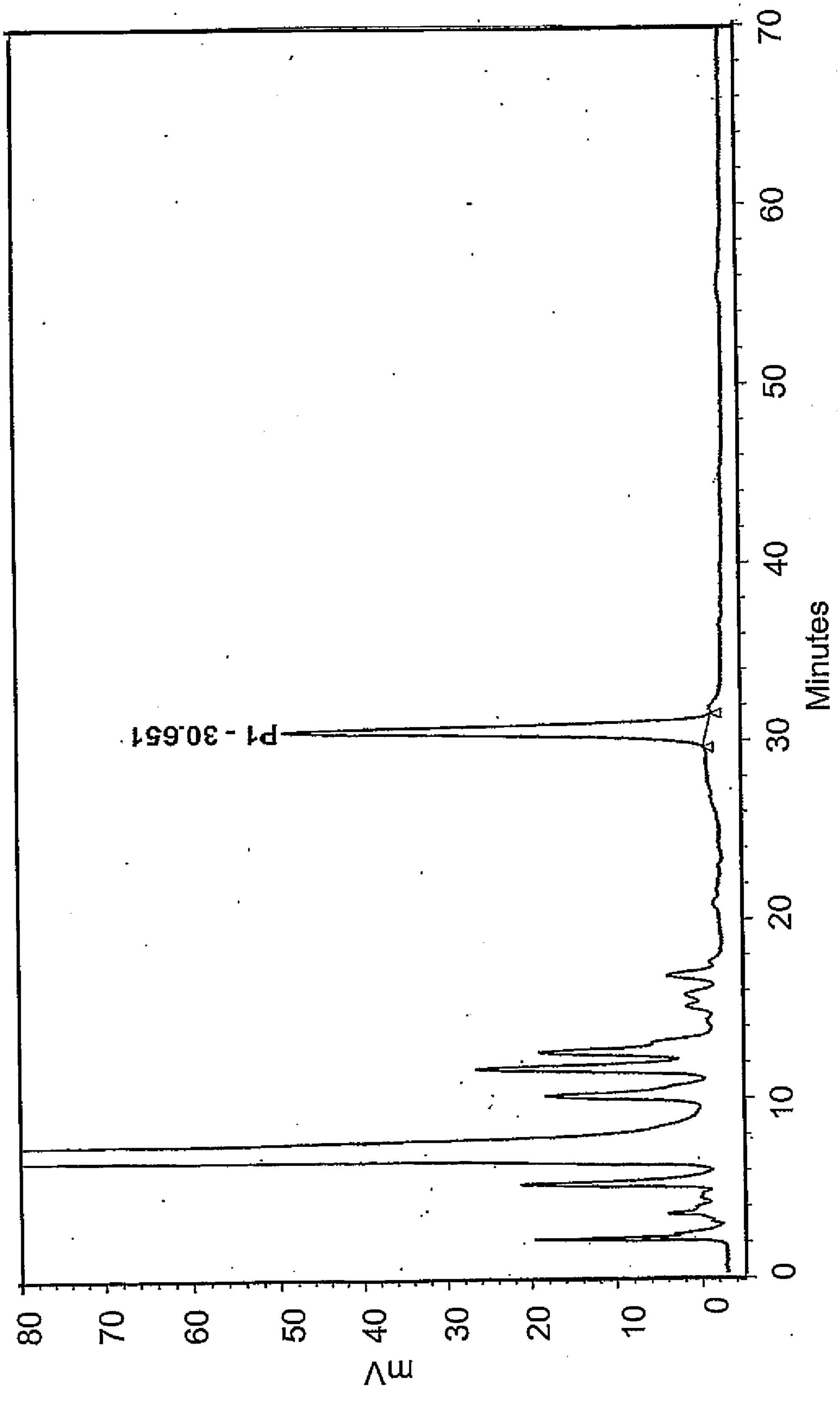


FIG. 91

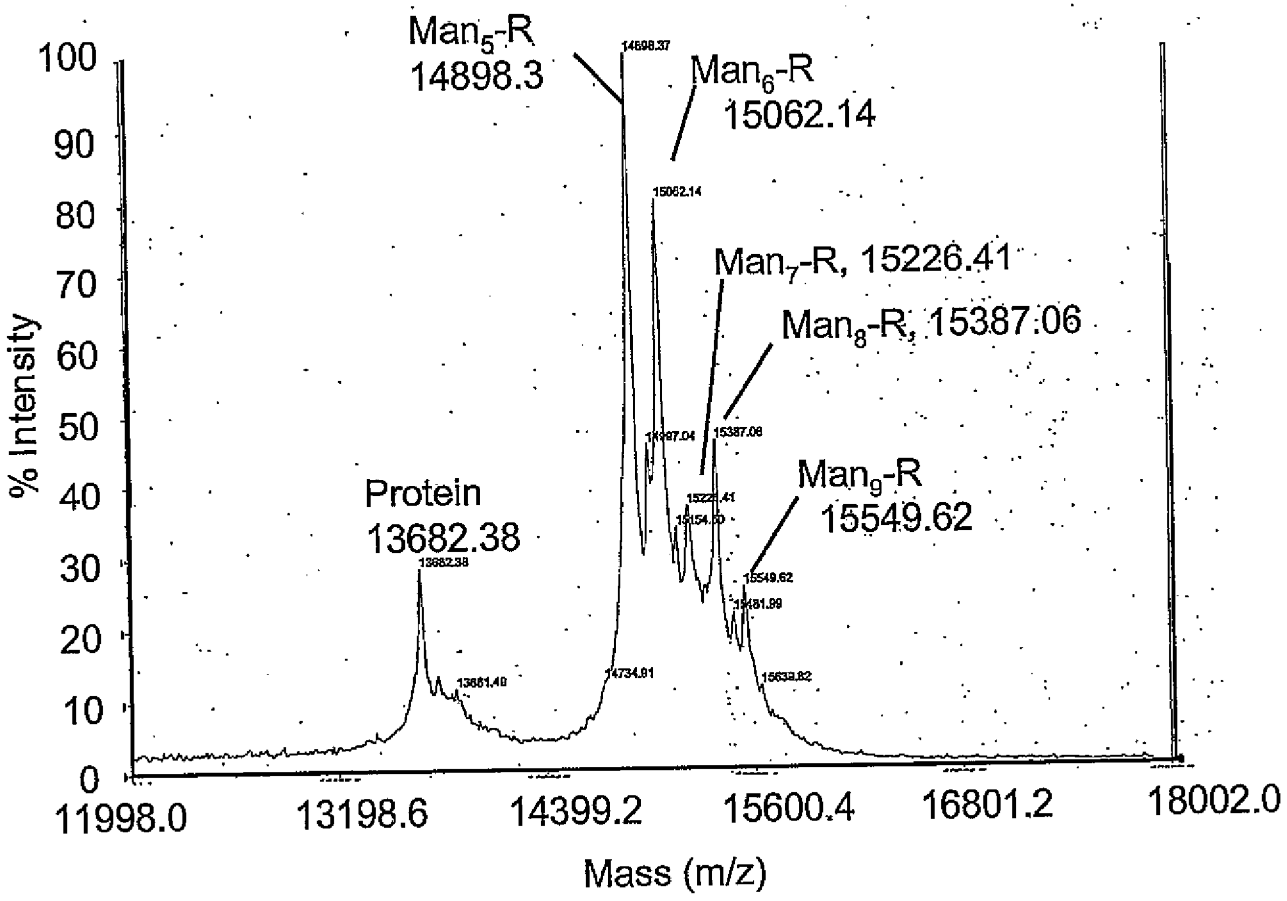

Man5-R
14898.3
Man6-R
15062.14
Man7-R, 15226.41
Man8-R, 15387.06
Man9-R
15549.62
Protein
13682.38
14898.37
15062.14
14987.04
15226.41
15154.50
15387.06
15549.62
15481.99
15639.82
14734.91
13682.38
13861.48
% Intensity
100
90
80
70
60
50
40
30
20
10
0
11998.0
13198.6
14399.2
15600.4
16801.2
18002.0
Mass (m/z)

FIG. 92A

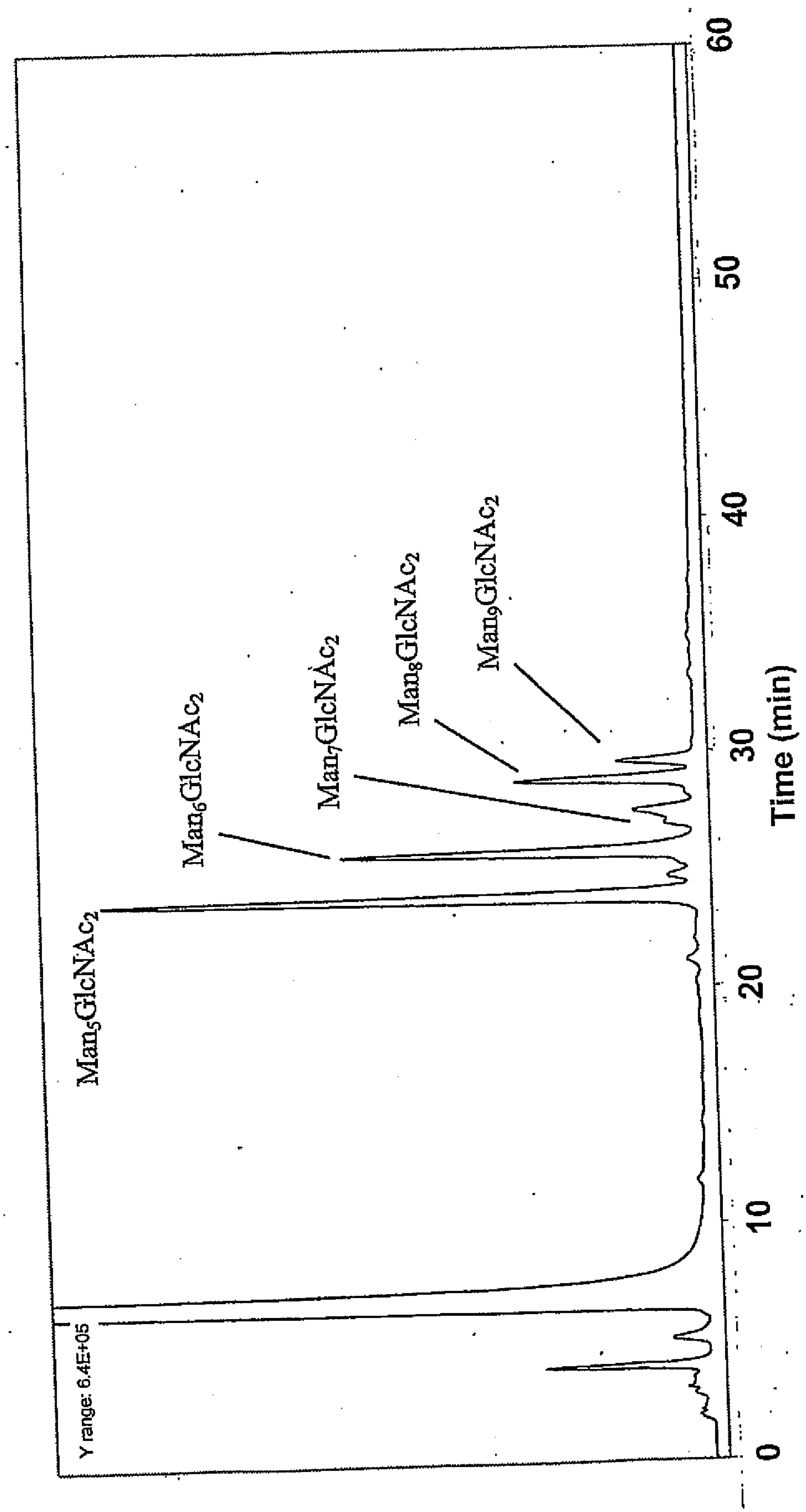

Y range: 6.4E+05
$Man_5GlcNAc_2$
$Man_6GlcNAc_2$
$Man_7GlcNAc_2$
$Man_8GlcNAc_2$
$Man_9GlcNAc_2$
0
10
20
30
40
50
60
Time (min)

FIG. 92B

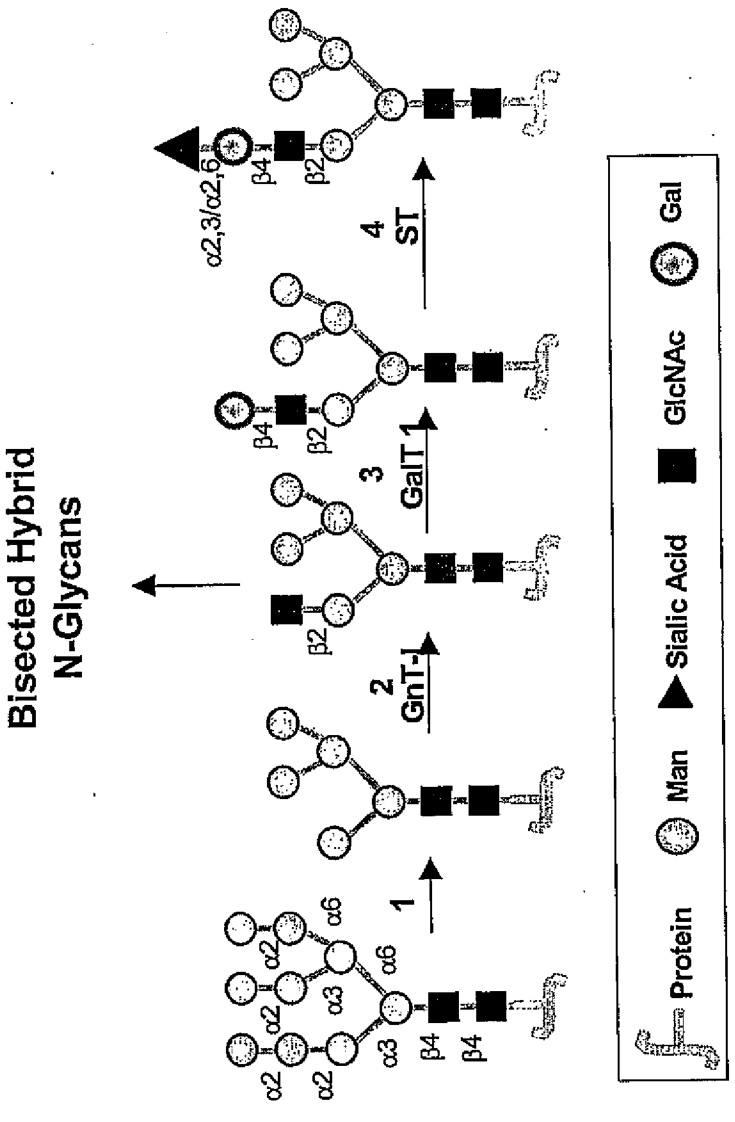

Bisected Hybrid
N-Glycans
α2
α2
α2
α2
α3
α3
α6
α6
β4
β4
1
2
GnT-I
β2
3
GalT 1
β4
β2
4
ST
α2,3/α2,6
β4
β2
Protein
Man
Sialic Acid
GlcNAc
Gal

FIG. 93

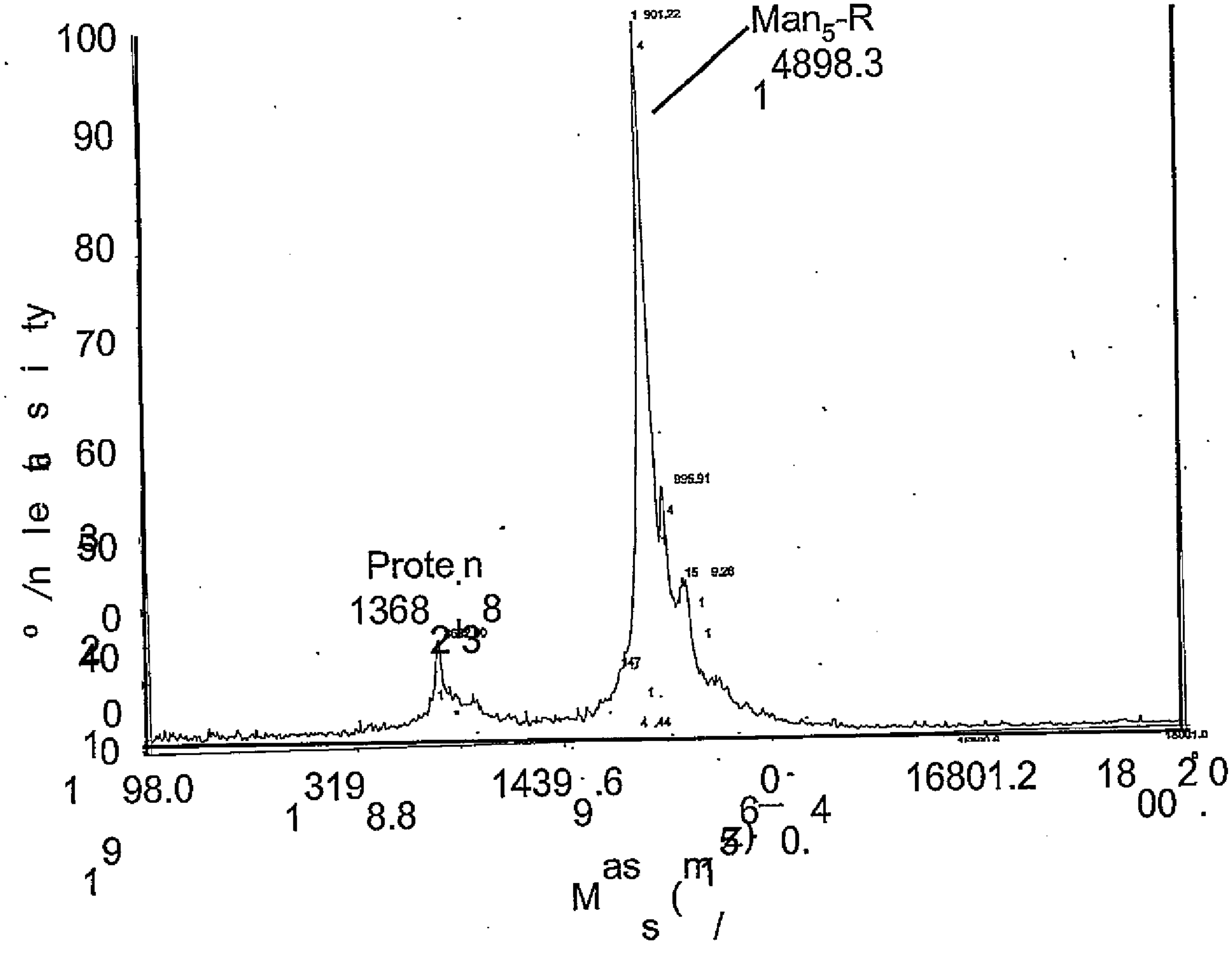

100
90
80
70
60
50
40
30
20
10
0
% Intensity
Man5-R
14898.3
Prote n
13688.23
98.0
13198.8
14399.6
16801.2
18002.0
Mass (m/z)

FIG. 94A

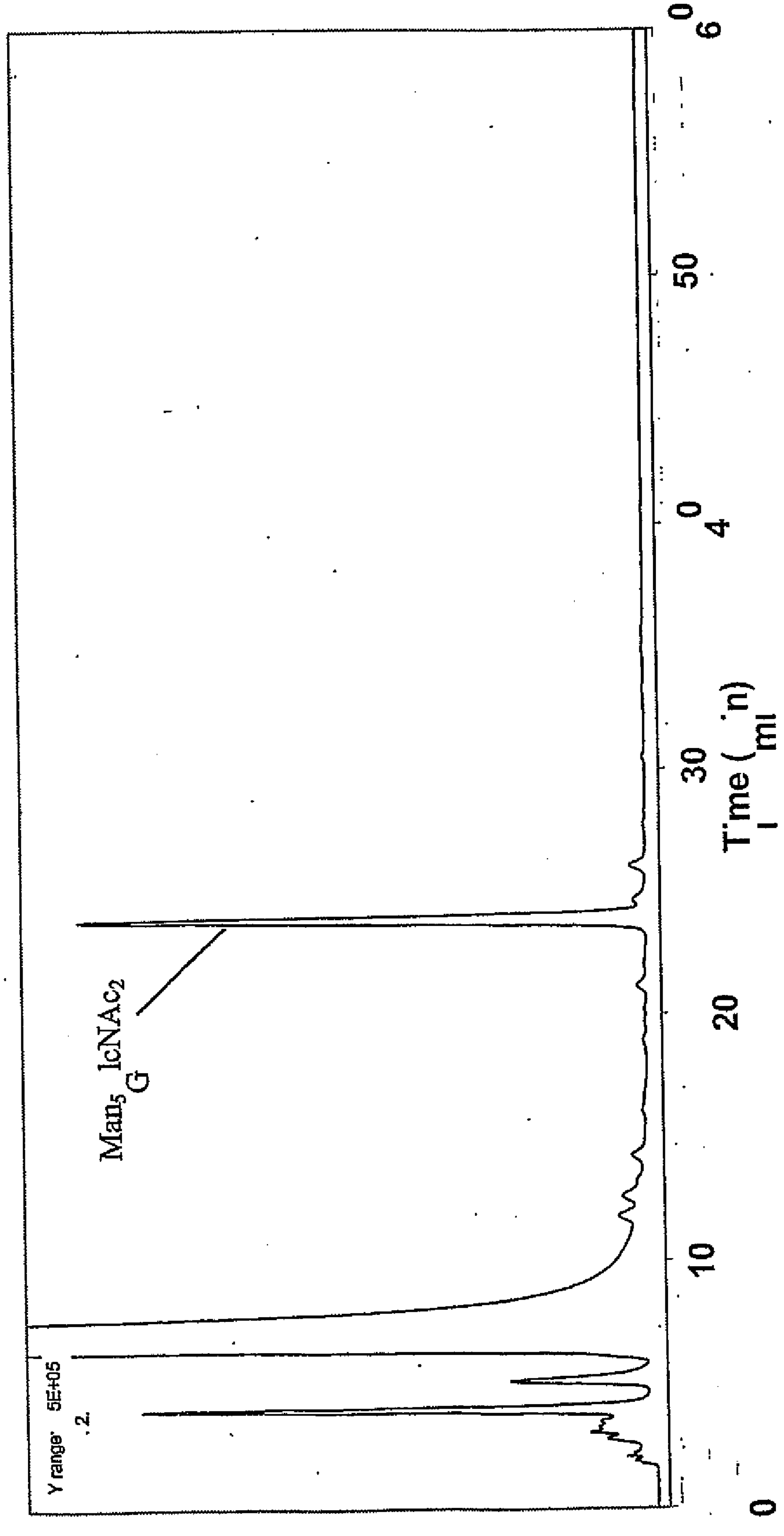


FIG. 94B

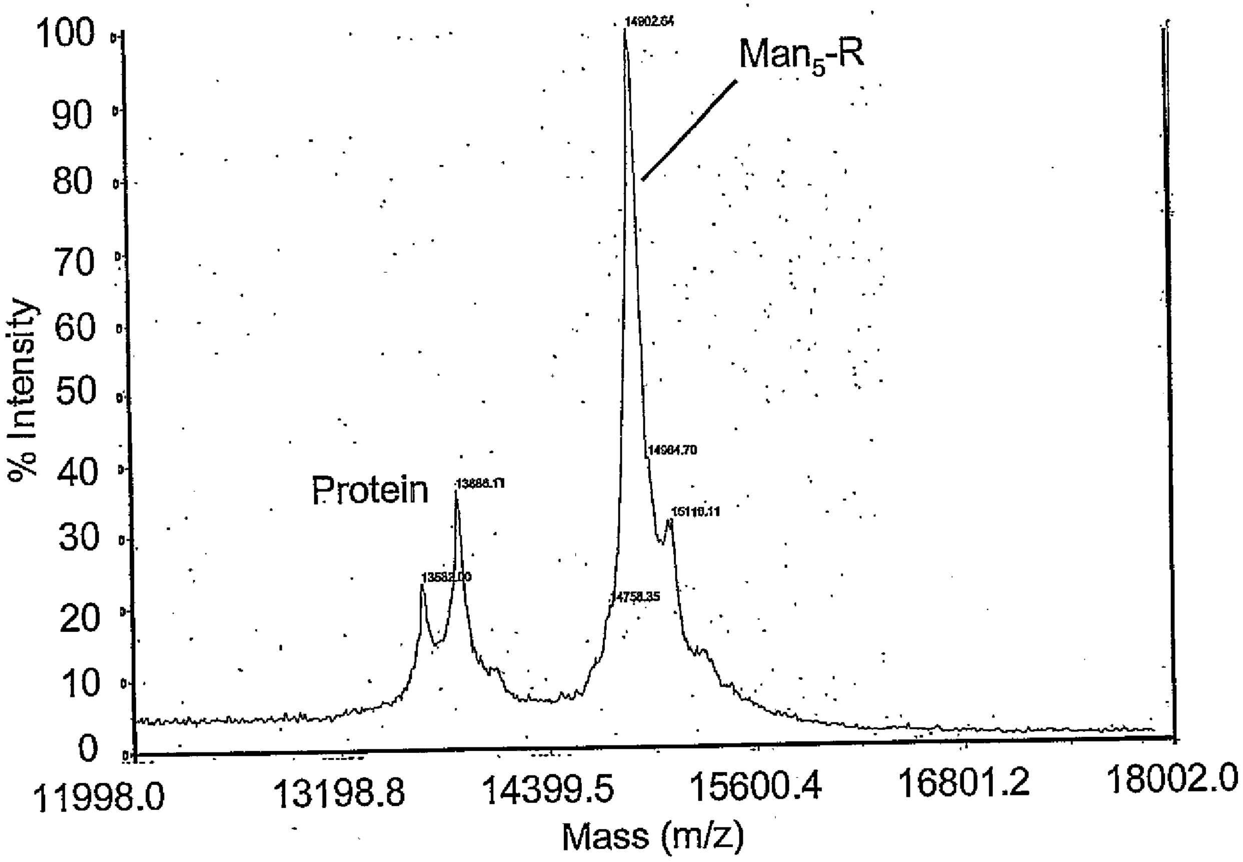

100
90
80
70
60
50
40
30
20
10
0
% Intensity
11998.0
13198.8
14399.5
15600.4
16801.2
18002.0
Mass (m/z)
Protein
Man_5-R
14902.64
14964.70
15116.11
14758.35
13888.11
13582.00

FIG. 95

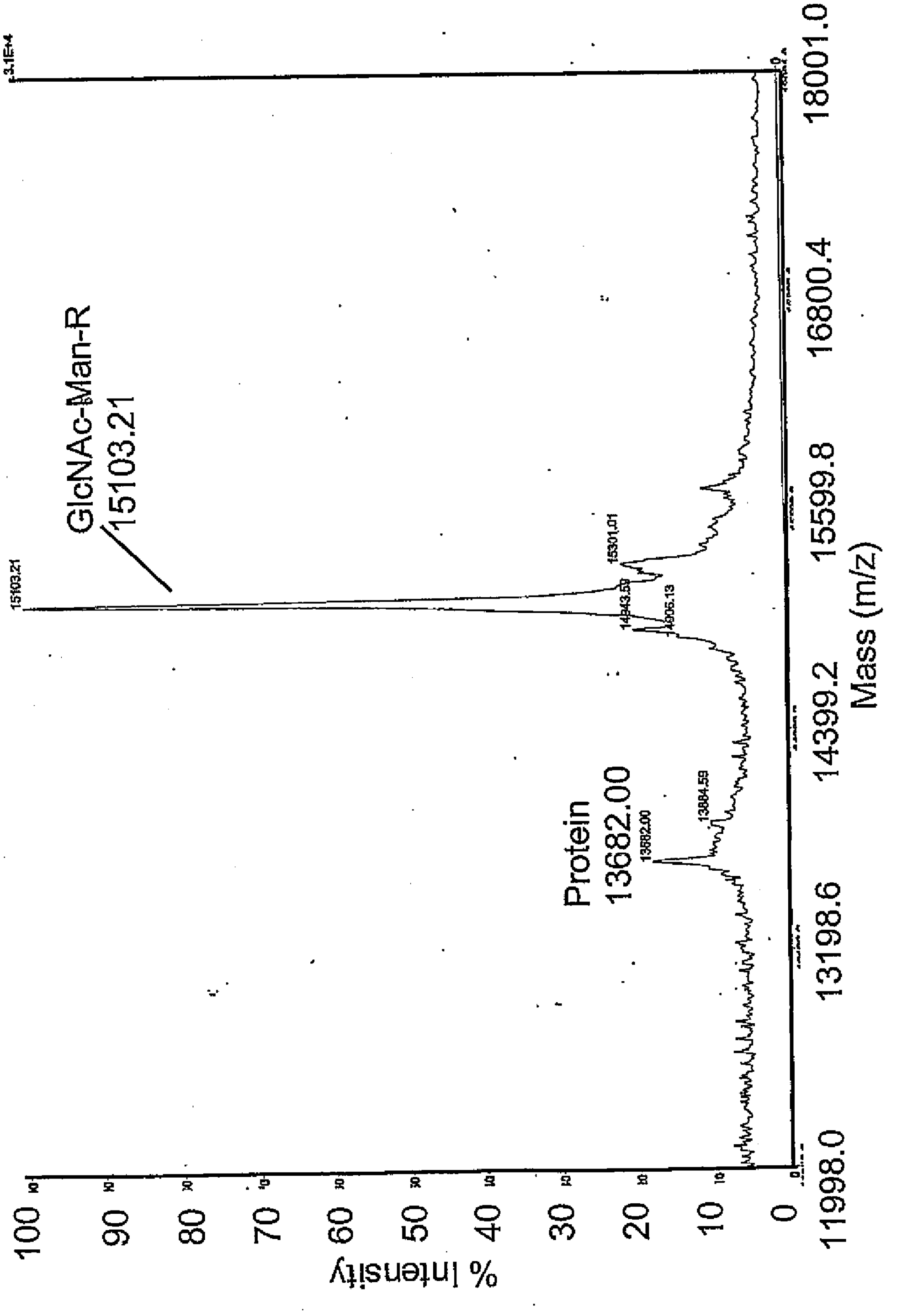

GlcNAc-Man-R
15103.21
Protein
13682.00
15103.21
15301.01
14943.59
14905.13
13682.00
13884.59
3.1E+4
% Intensity
100
90
80
70
60
50
40
30
20
10
0
11998.0
13198.6
14399.2
15599.8
16800.4
18001.0
Mass (m/z)

FIG. 96

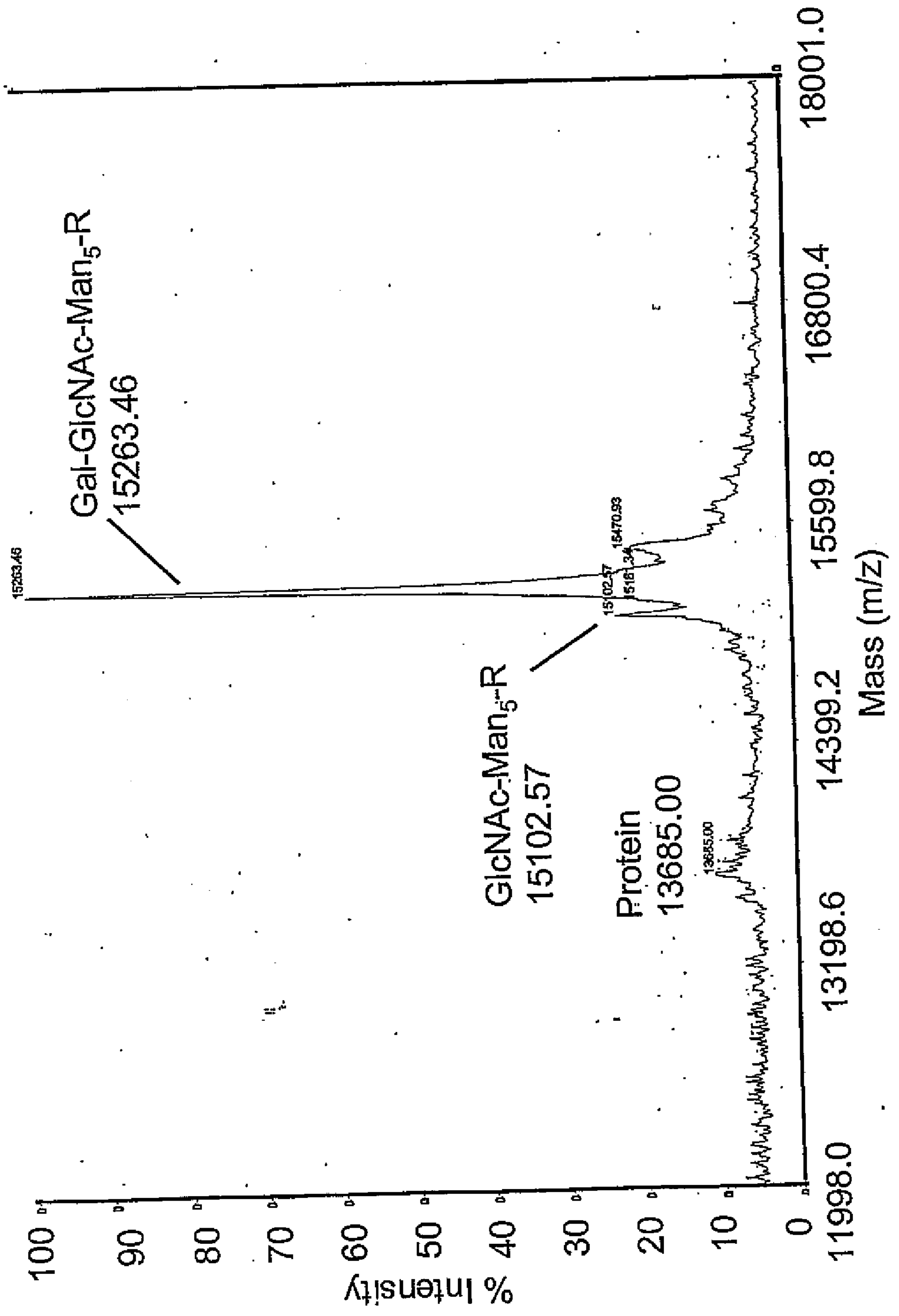

Gal-GlcNAc-Man5-R
15263.46
GlcNAc-Man5-R
15102.57
Protein
13685.00
15263.46
15102.57
15161.34
15470.93
13685.00
% Intensity
100
90
80
70
60
50
40
30
20
10
0
11998.0
13198.6
14399.2
15599.8
16800.4
18001.0
Mass (m/z)

FIG. 97

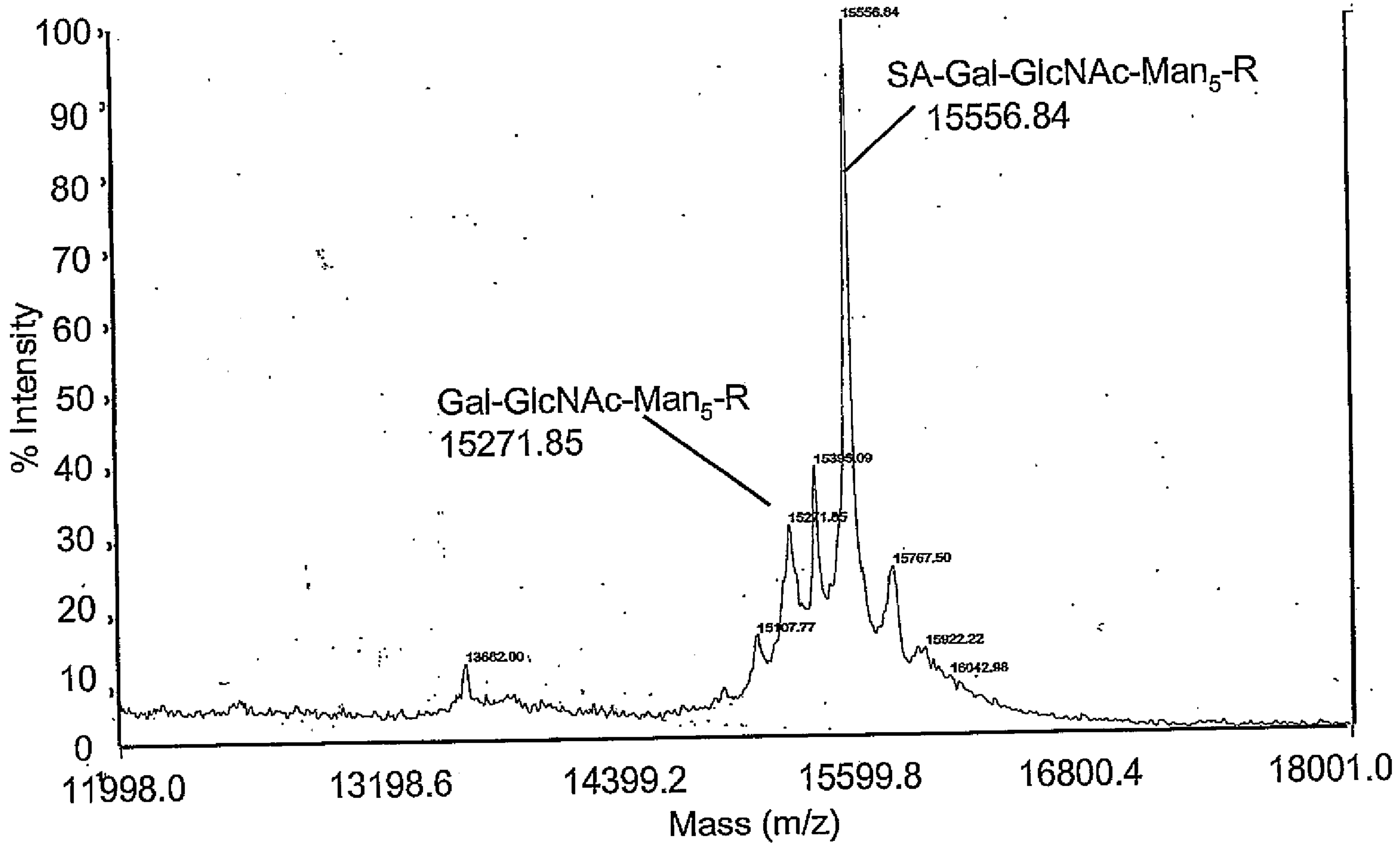

% Intensity
100
90
80
70
60
50
40
30
20
10
0
11998.0
13198.6
14399.2
15599.8
16800.4
18001.0
Mass (m/z)
SA-Gal-GlcNAc-Man_5-R
15556.84
Gal-GlcNAc-Man_5-R
15271.85
15556.84
15395.09
15271.85
15107.77
15767.50
15922.22
16042.98
13682.00

FIG. 98

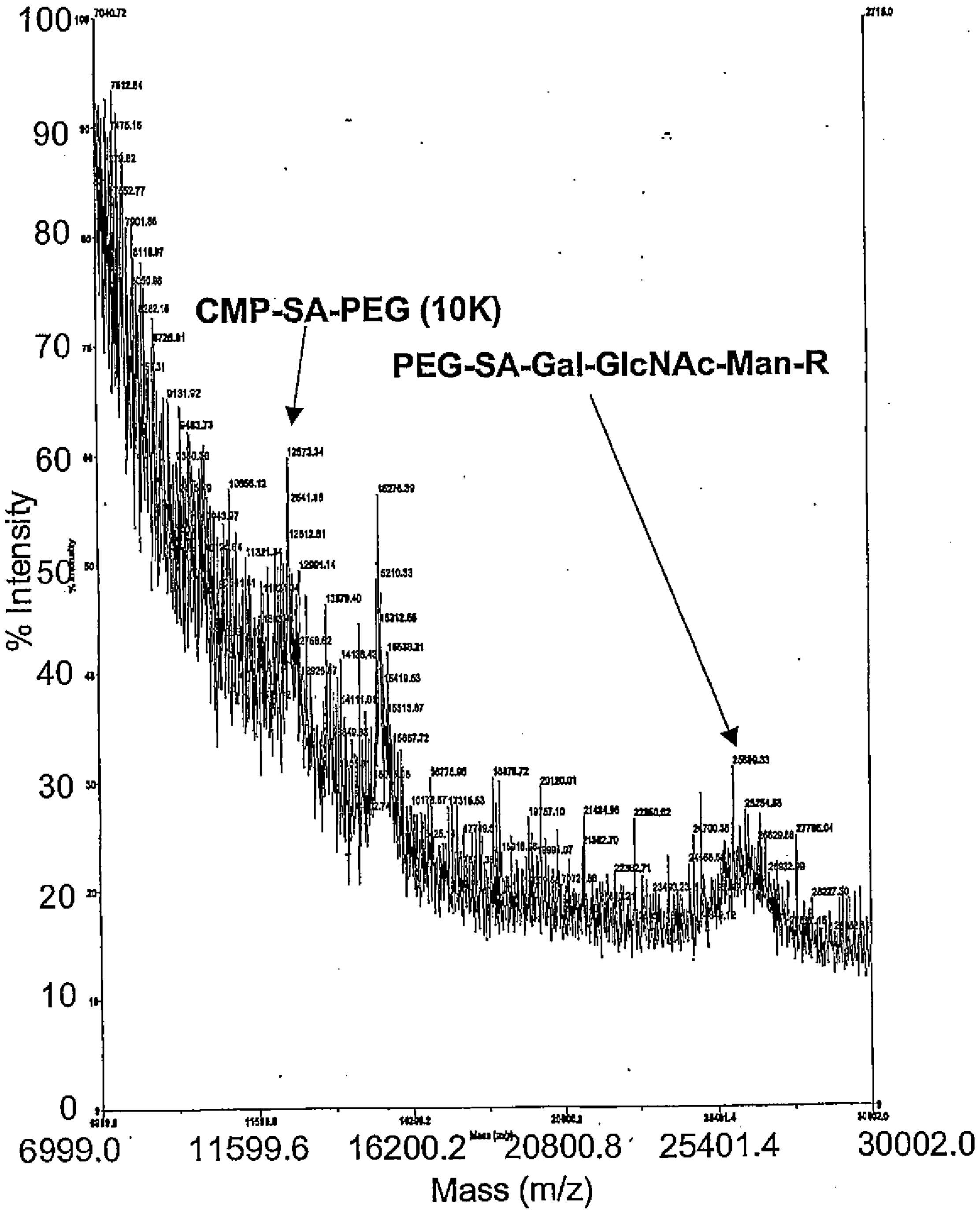

CMP-SA-PEG (10K)
PEG-SA-Gal-GlcNAc-Man-R
% Intensity
100
90
80
70
60
50
40
30
20
10
0
6999.0
11599.6
16200.2
20800.8
25401.4
30002.0
Mass (m/z)

FIG. 99A

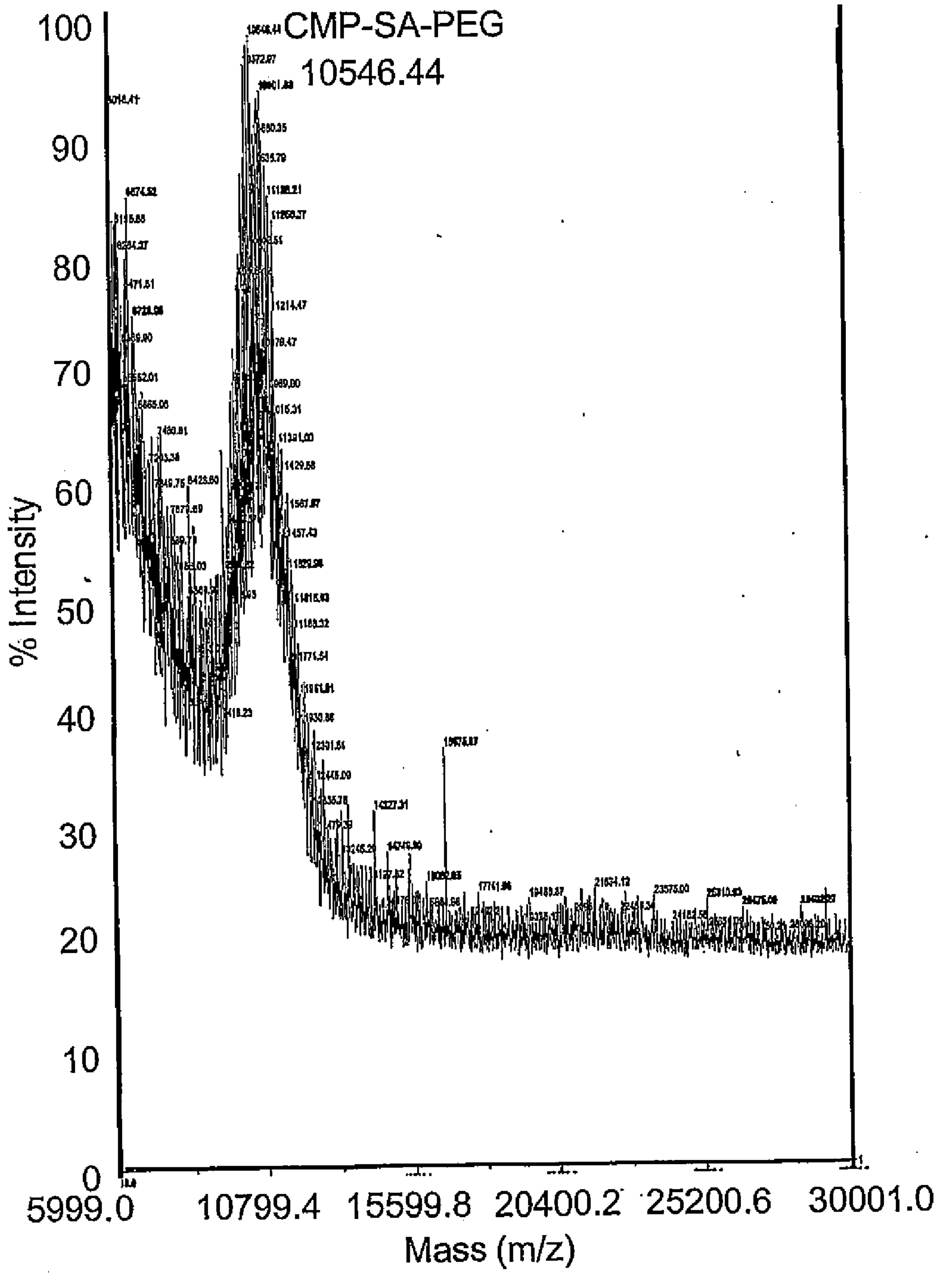

CMP-SA-PEG
10546.44
% Intensity
100
90
80
70
60
50
40
30
20
10
0
5999.0
10799.4
15599.8
20400.2
25200.6
30001.0
Mass (m/z)

FIG. 99B

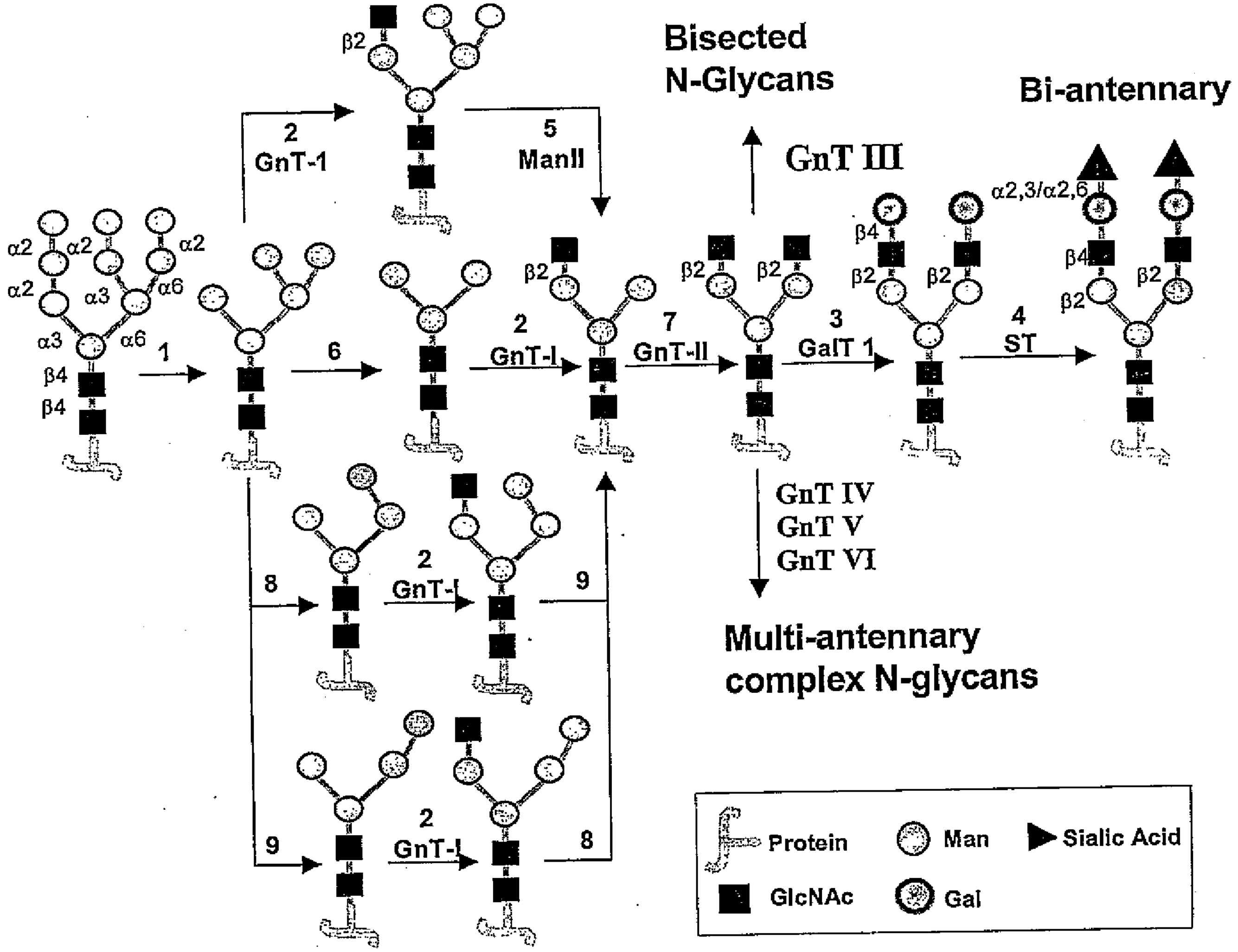

α2
α2
α2
α2
α3
α6
α3
α6
β4
β4
1
6
2
GnT-1
β2
5
ManII
2
GnT-I
β2
7
GnT-II
β2
β2
Bisected
N-Glycans
GnT III
3
GalT 1
β4
β2
β2
4
ST
α2,3/α2,6
β4
β2
β2
Bi-antennary
GnT IV
GnT V
GnT VI
Multi-antennary
complex N-glycans
8
2
GnT-I
9
9
2
GnT-I
8
Protein
Man
Sialic Acid
GlcNAc
Gal

FIG. 100

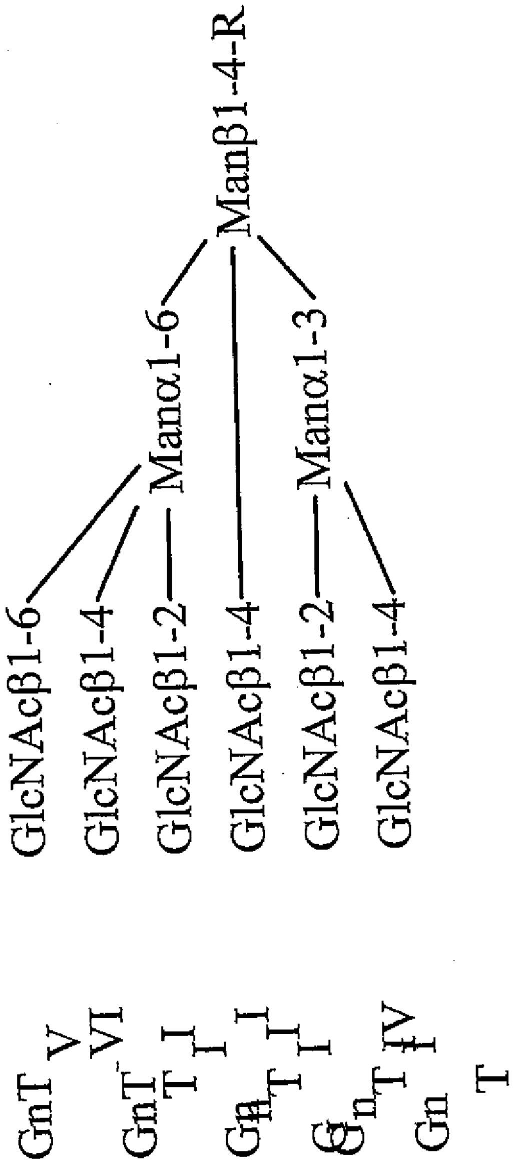

Manβ1-4-R
Manα1-6
Manα1-3
GlcNAcβ1-6
GlcNAcβ1-4
GlcNAcβ1-2
GlcNAcβ1-4
GlcNAcβ1-2
GlcNAcβ1-4
GnT V
GnT VI
GnT II
GnT III
GnT I
GnT IV

FIG. 101

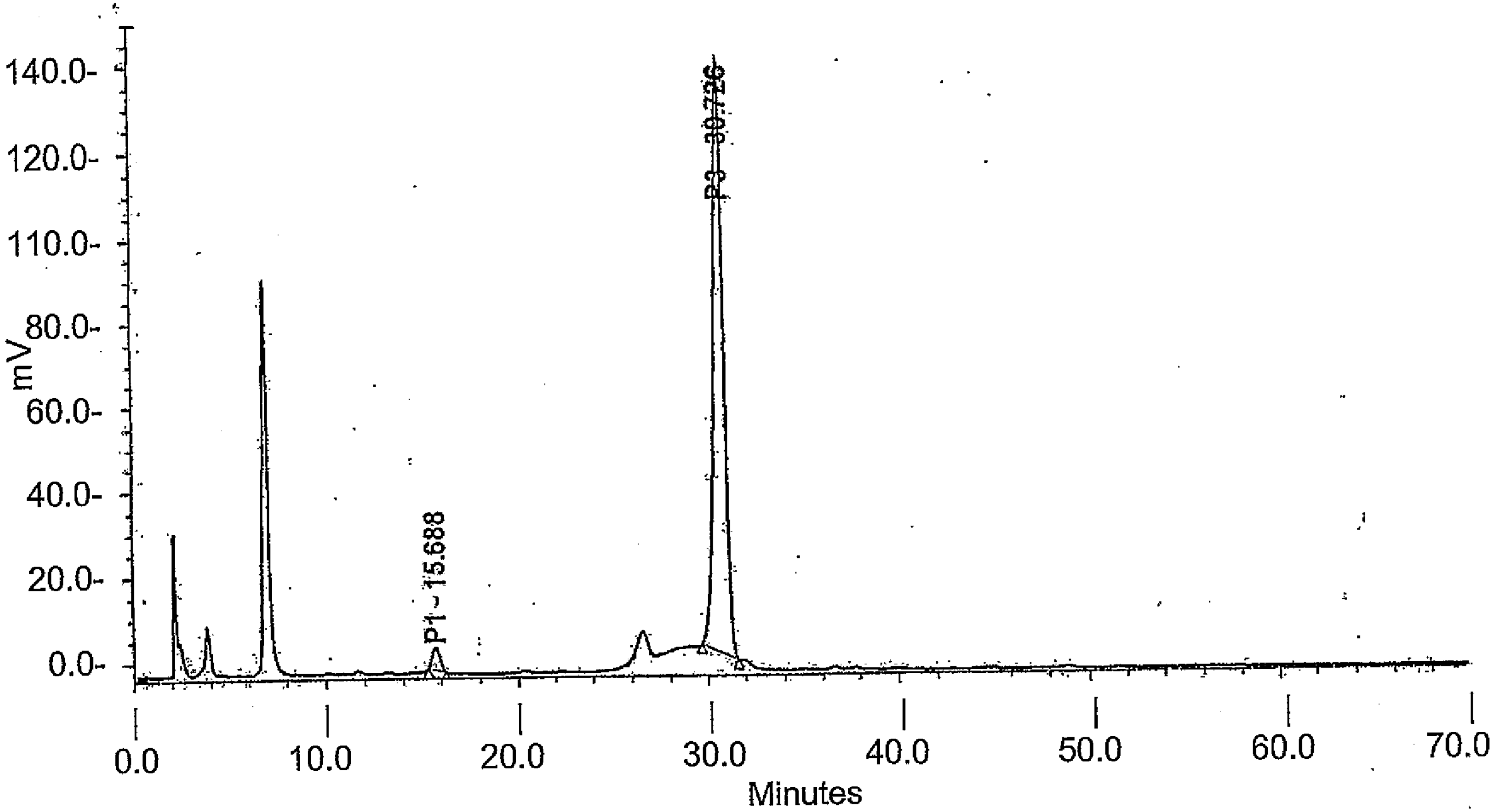

mV
140.0-
120.0-
110.0-
80.0-
60.0-
40.0-
20.0-
0.0-
P1 - 15.688
P3 - 30.726
0.0
10.0
20.0
30.0
40.0
50.0
60.0
70.0
Minutes

FIG. 102A

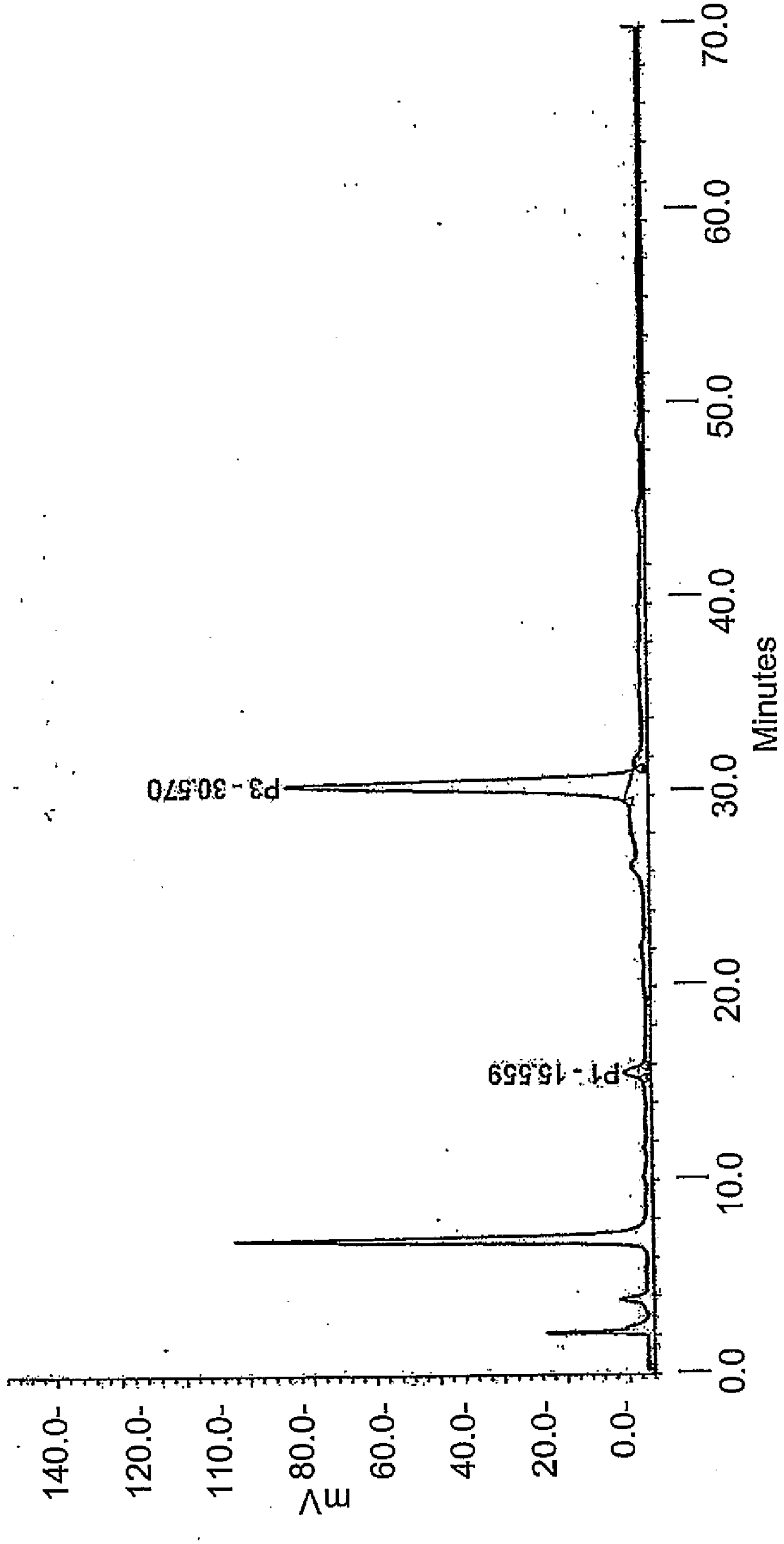

P3 - 30.570
P1 - 15.559
Minutes
0.0
10.0
20.0
30.0
40.0
50.0
60.0
70.0
mV
140.0
120.0
110.0
80.0
60.0
40.0
20.0
0.0

FIG. 102B

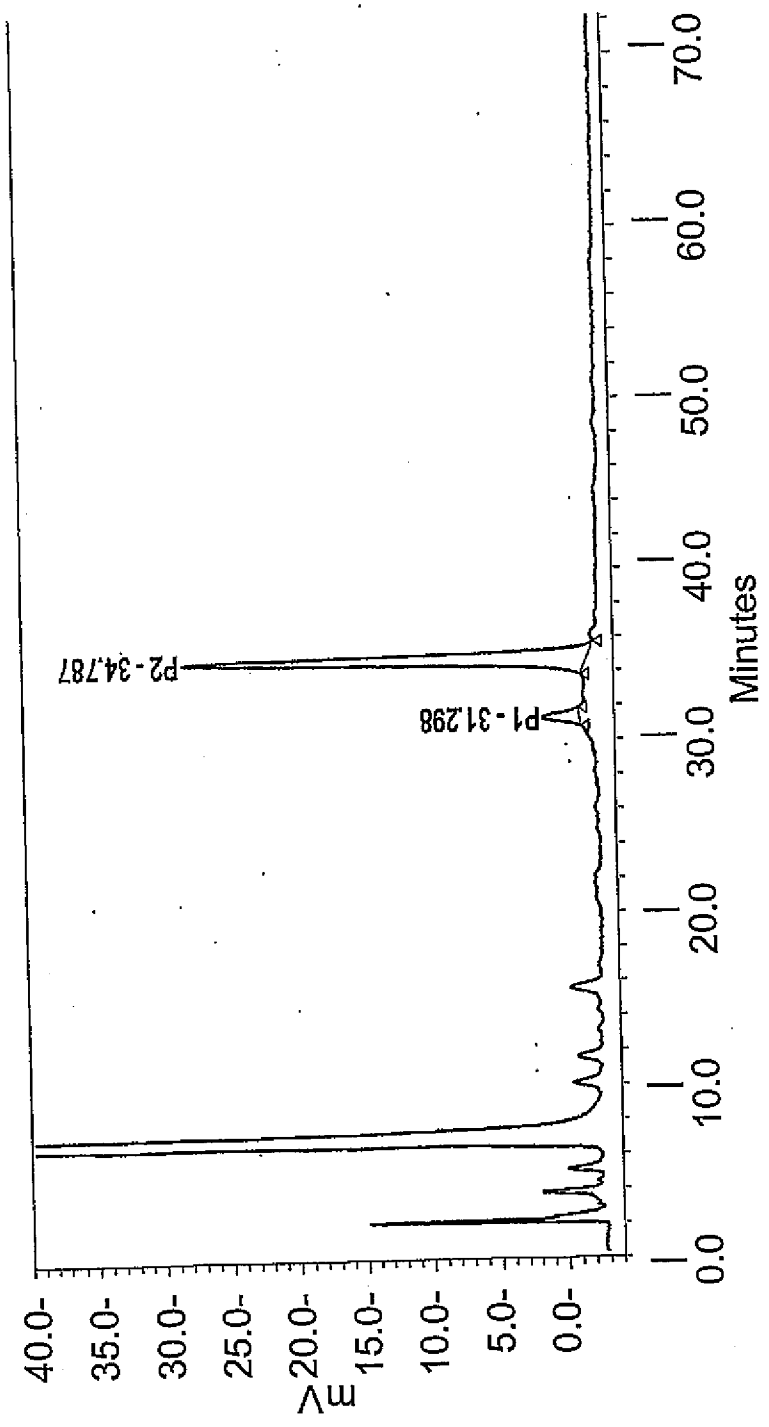

mV
40.0-
35.0-
30.0-
25.0-
20.0-
15.0-
10.0-
5.0-
0.0-
0.0
10.0
20.0
30.0
40.0
50.0
60.0
70.0
Minutes
P1 - 31.298
P2 - 34.787

FIG. 103

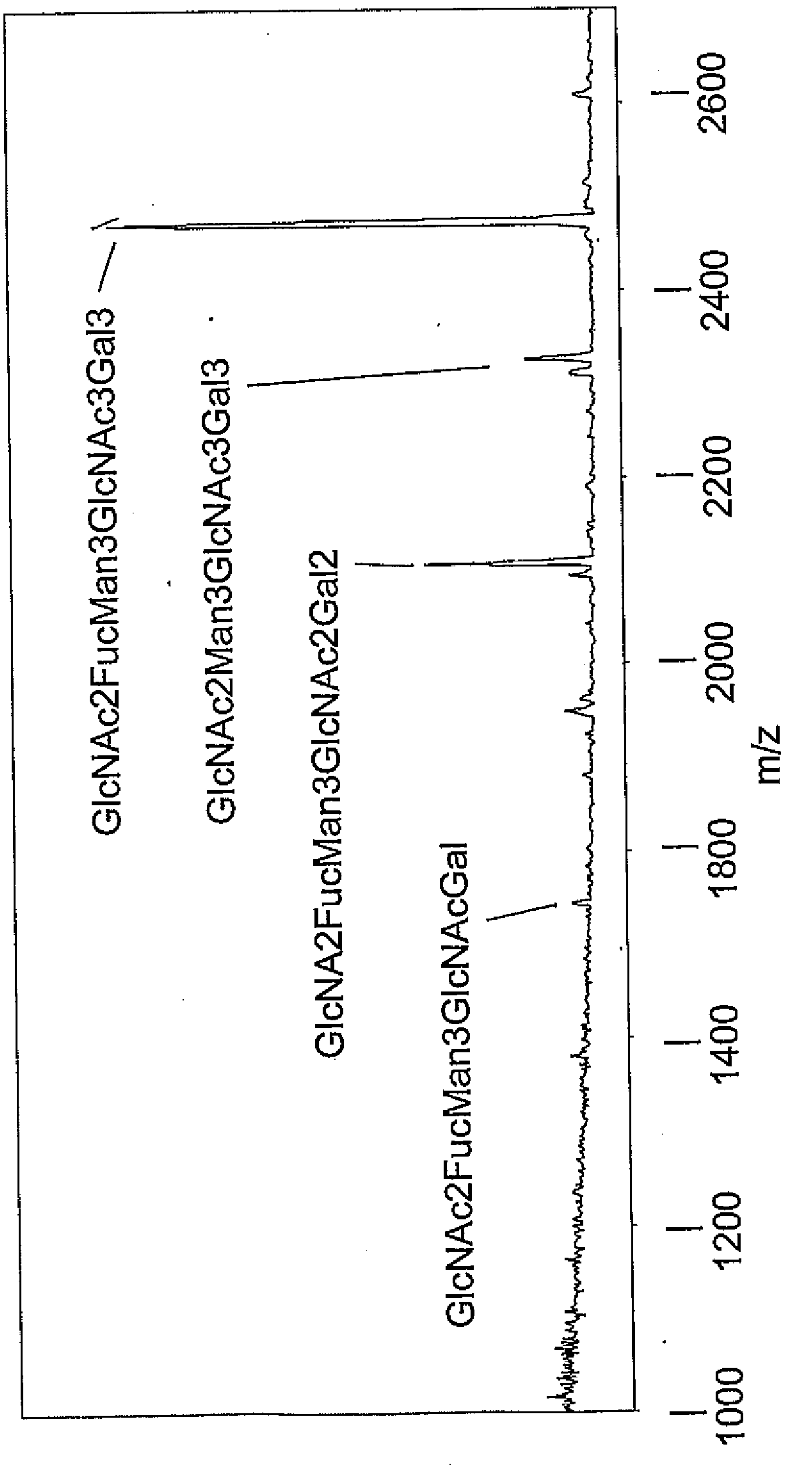

GlcNAc2FucMan3GlcNAc3Gal3
GlcNAc2Man3GlcNAc3Gal3
GlcNA2FucMan3GlcNAc2Gal2
GlcNAc2FucMan3GlcNAcGal
1000
1200
1400
1800
2000
2200
2400
2600
m/z

FIG. 104

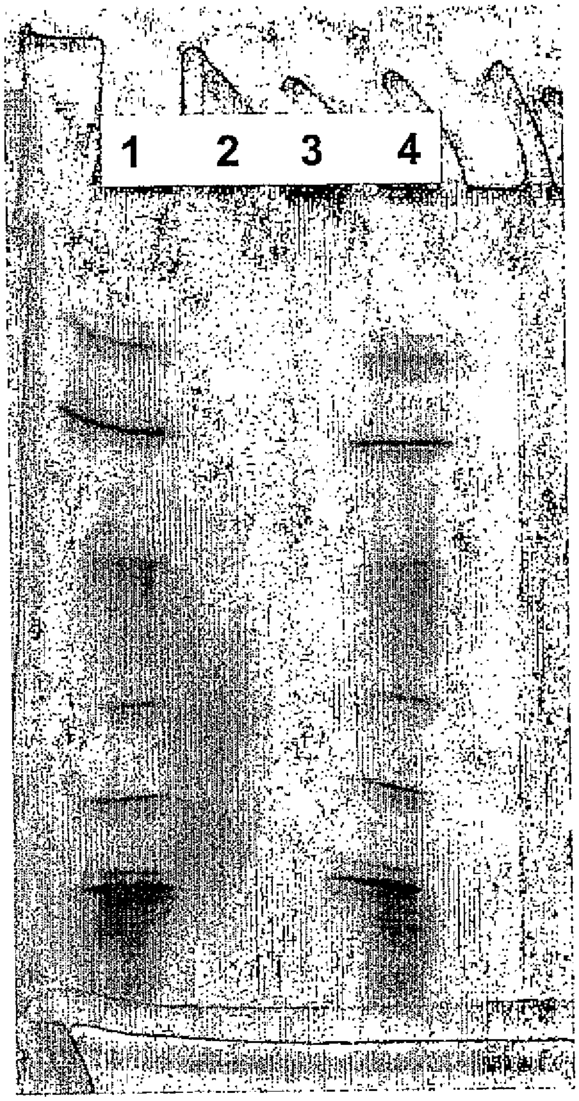


FIG. 105

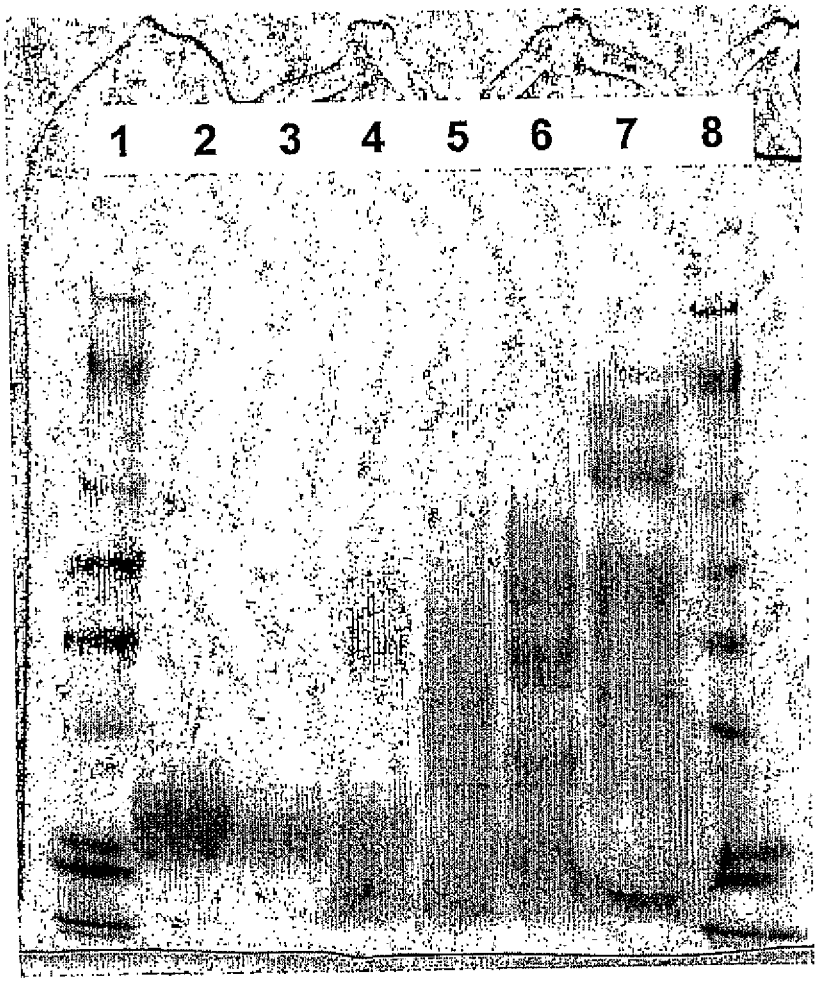


FIG. 106

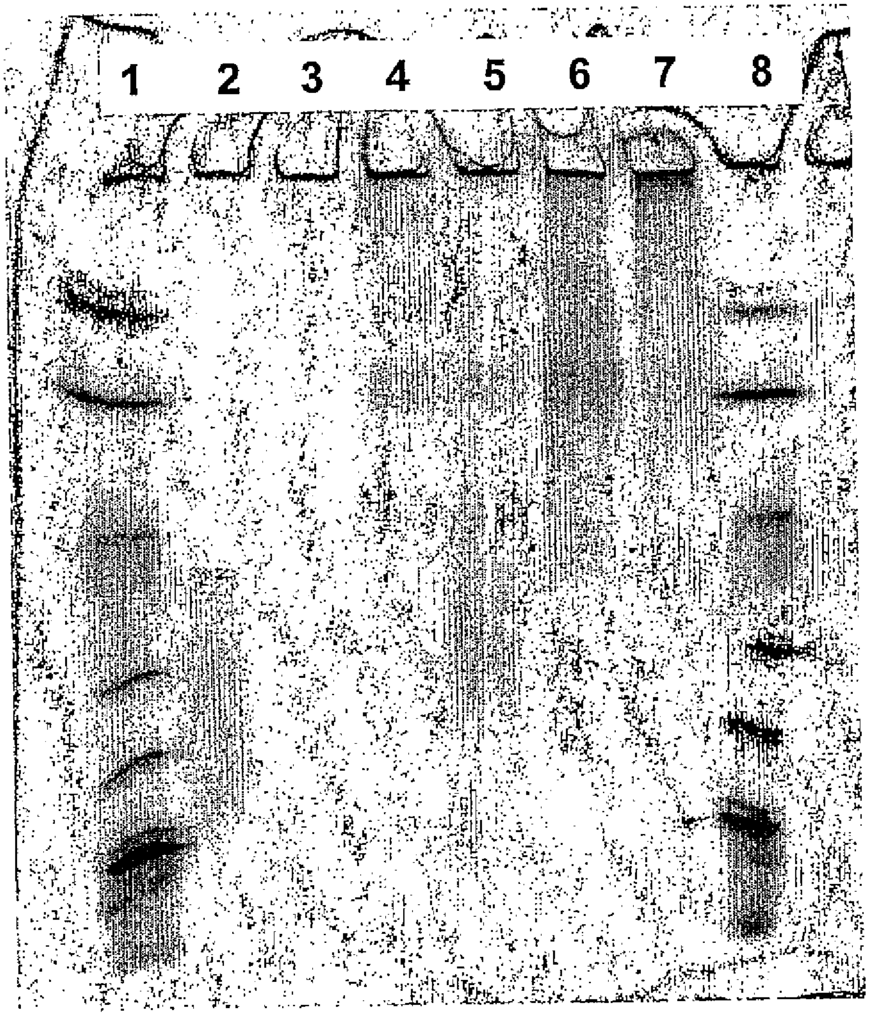


FIG. 107

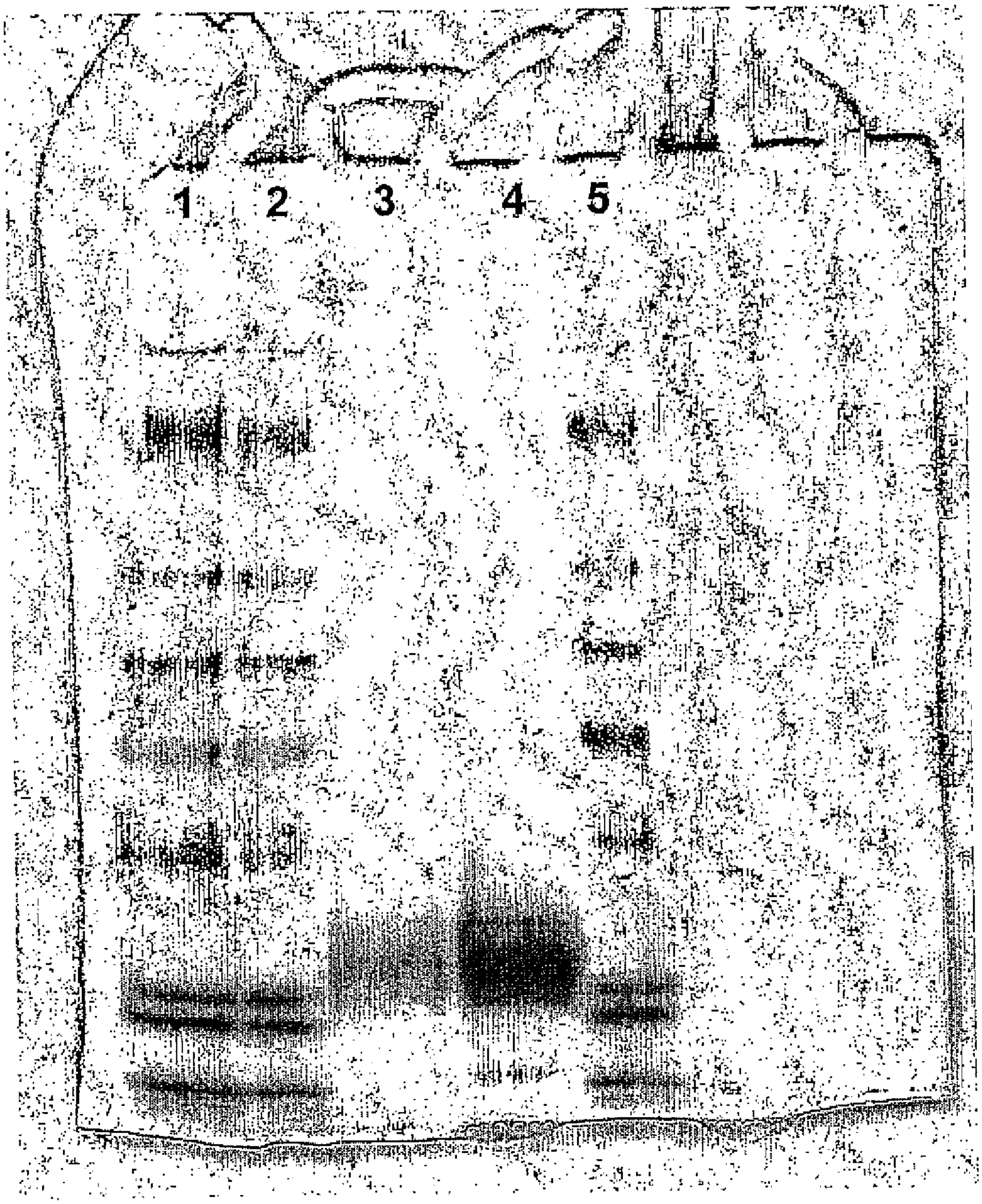


FIG. 108

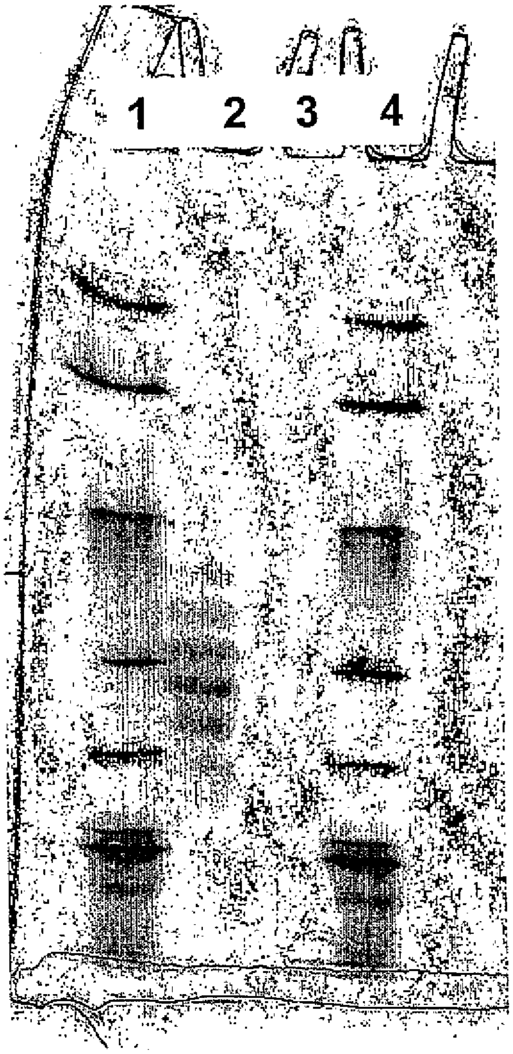


FIG. 109

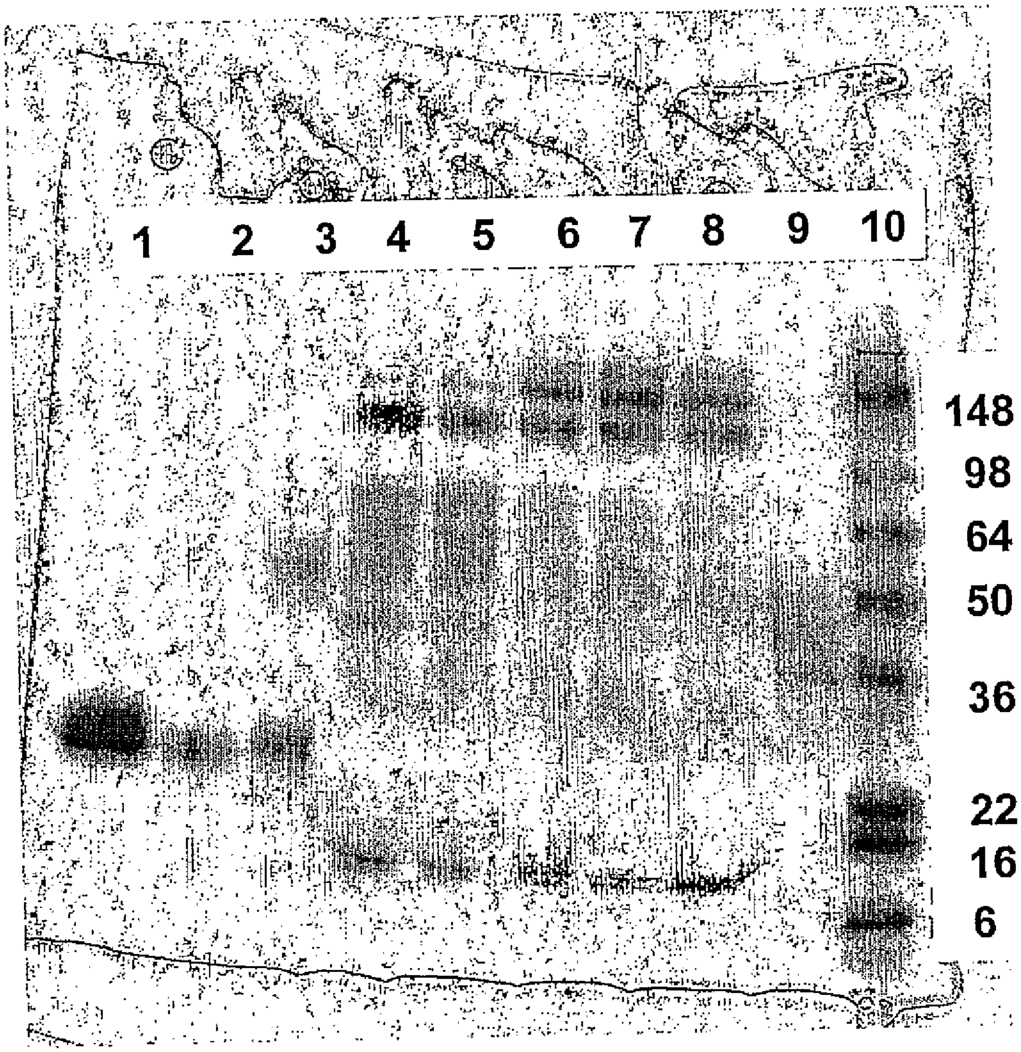


FIG. 110

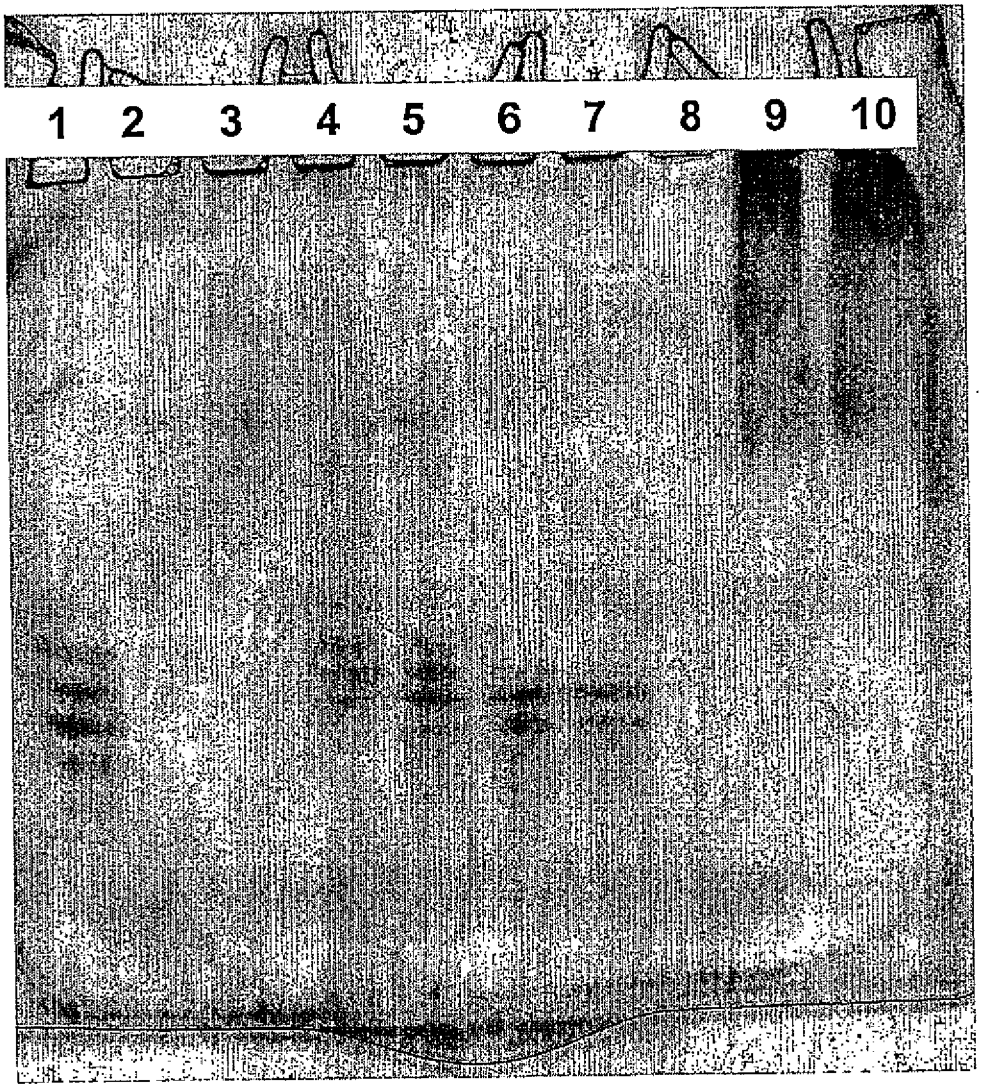


FIG. 111

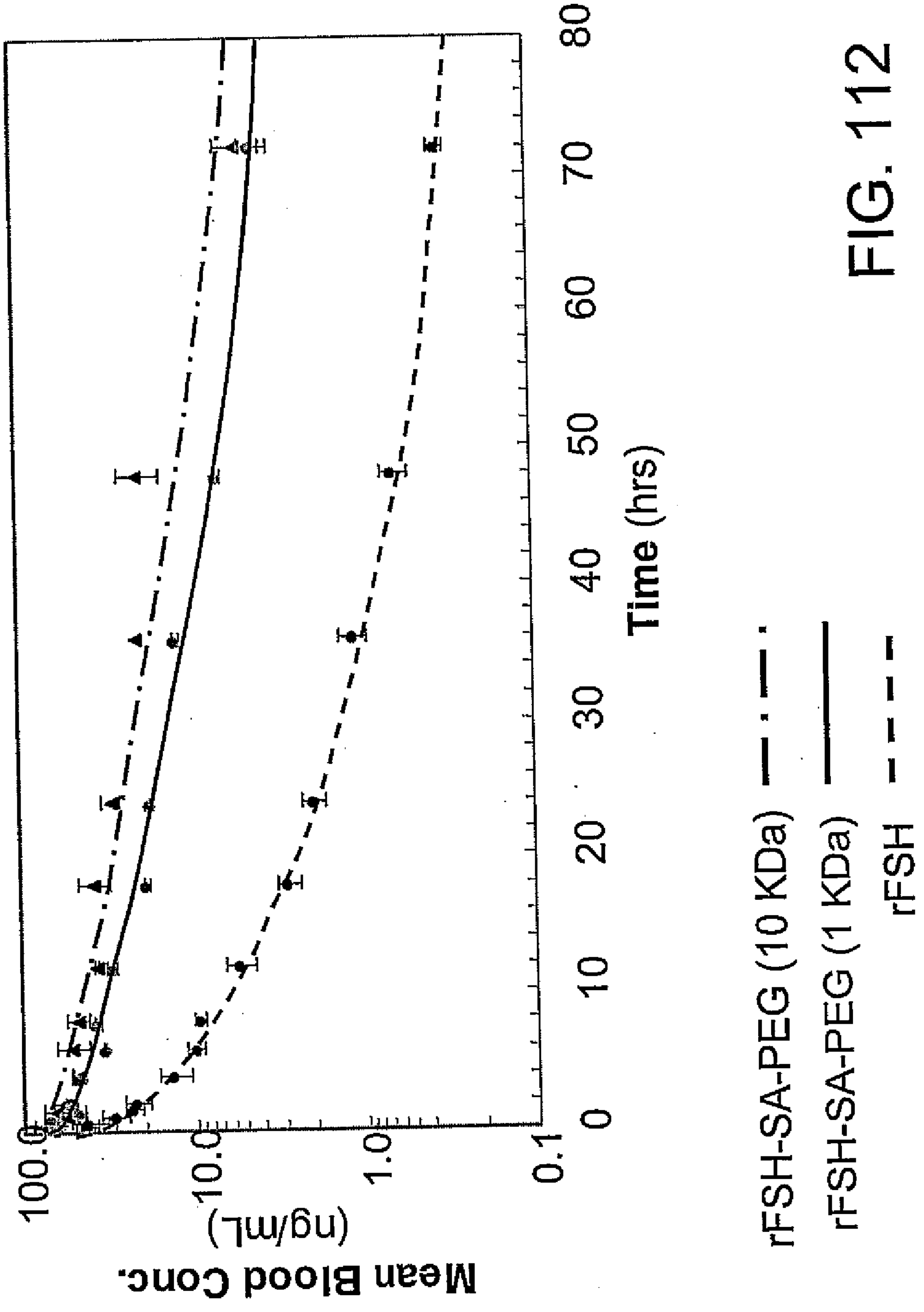

Mean Blood Conc. (ng/mL)
100.0
10.0
1.0
0.1
0
10
20
30
40
50
60
70
80
Time (hrs)
rFSH-SA-PEG (10 KDa)
rFSH-SA-PEG (1 KDa)
rFSH

FIG. 112

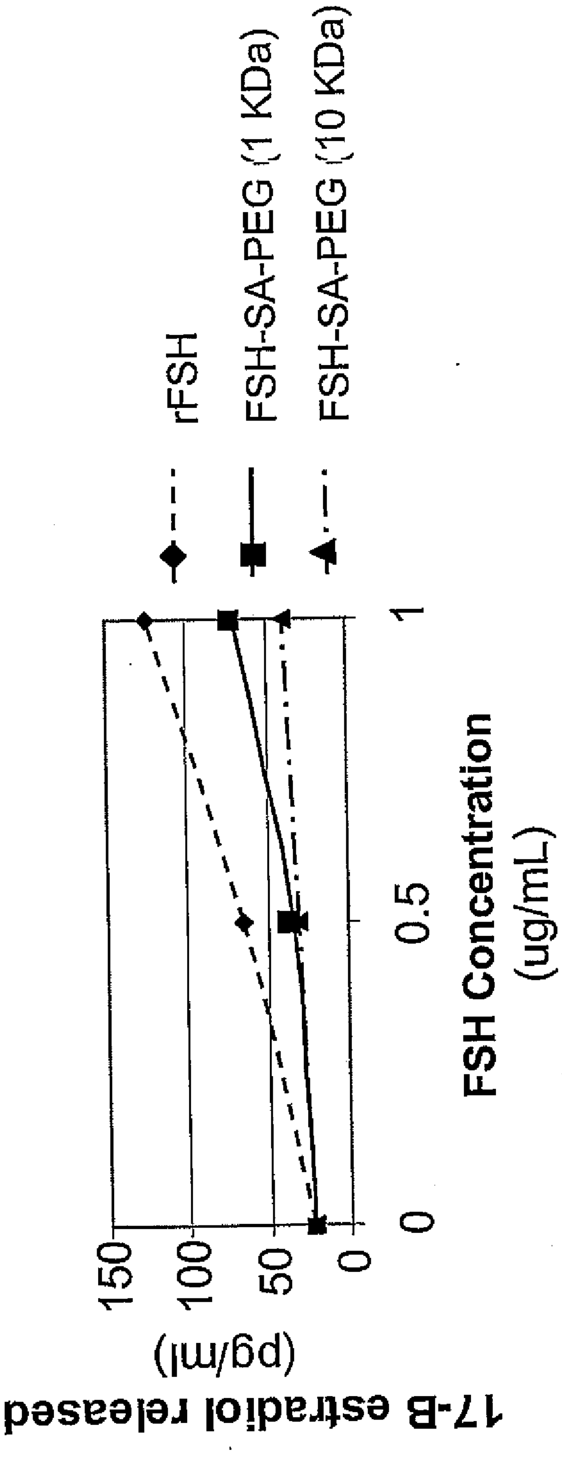

17-B estradiol released (pg/ml)
150
100
50
0
0
0.5
1
FSH Concentration (ug/mL)
rFSH
FSH-SA-PEG (1 KDa)
FSH-SA-PEG (10 KDa)

FIG. 113

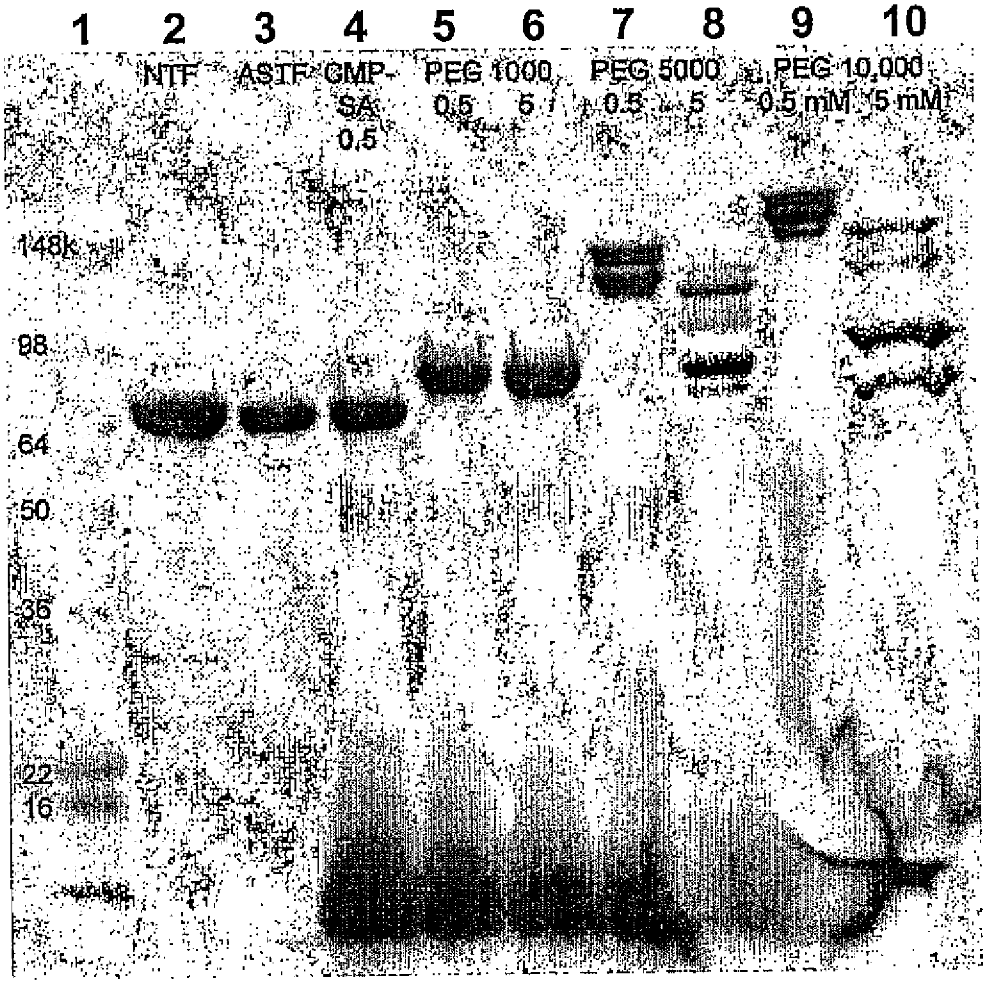

1
2
3
4
5
6
7
8
9
10
NTF
ASTF
GMP-SA 0.5
PEG 1000
0.5
5
PEG 5000
0.5
5
PEG 10,000
0.5 mM
5 mM
148k
98
64
50
36
22
16

FIG. 114

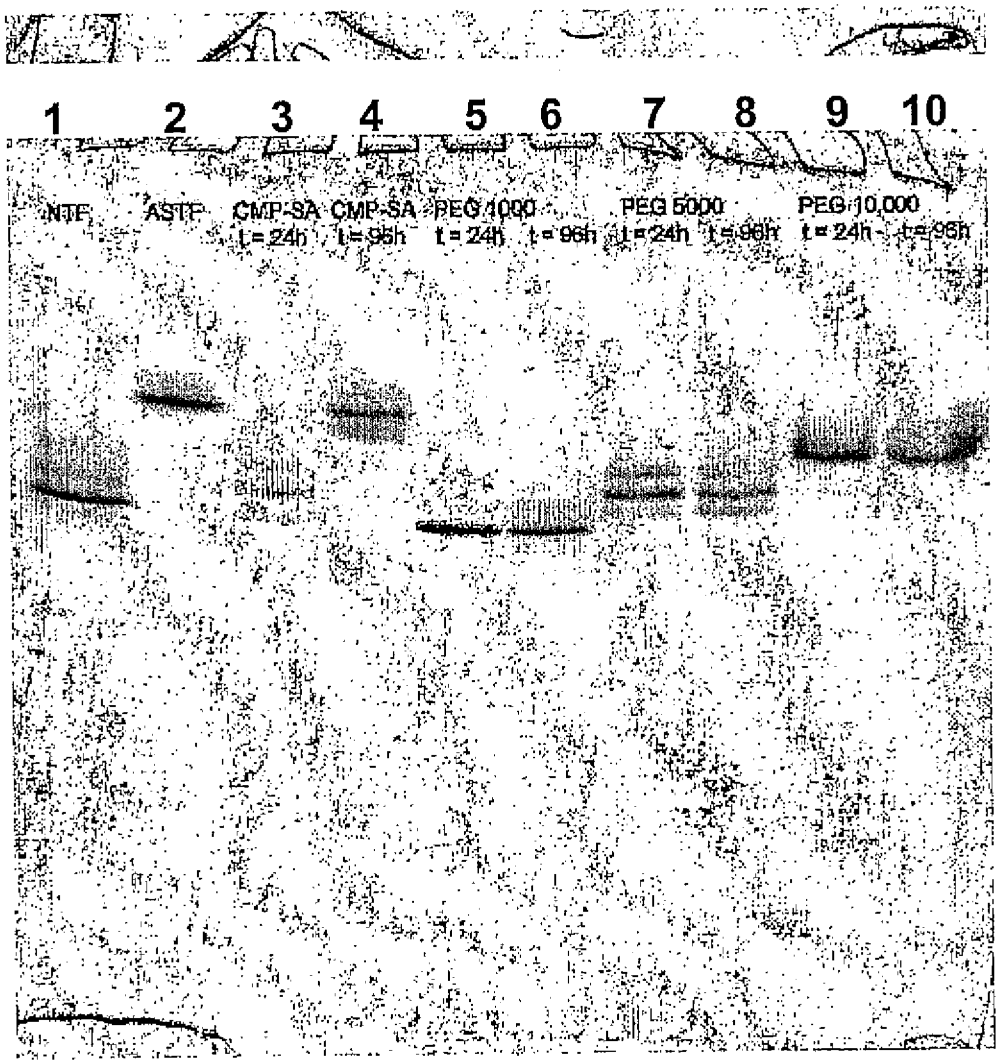

1
2
3
4
5
6
7
8
9
10
NTF
ASTF
CMP-SA
t = 24h
CMP-SA
t = 96h
PEG 1000
t = 24h
t = 96h
PEG 5000
t = 24h
t = 96h
PEG 10,000
t = 24h
t = 96h

FIG. 115

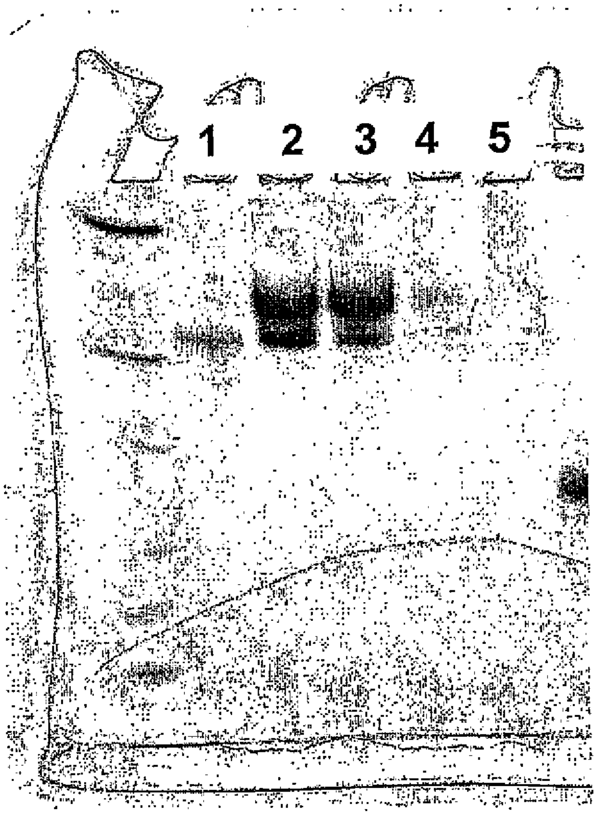


FIG. 116

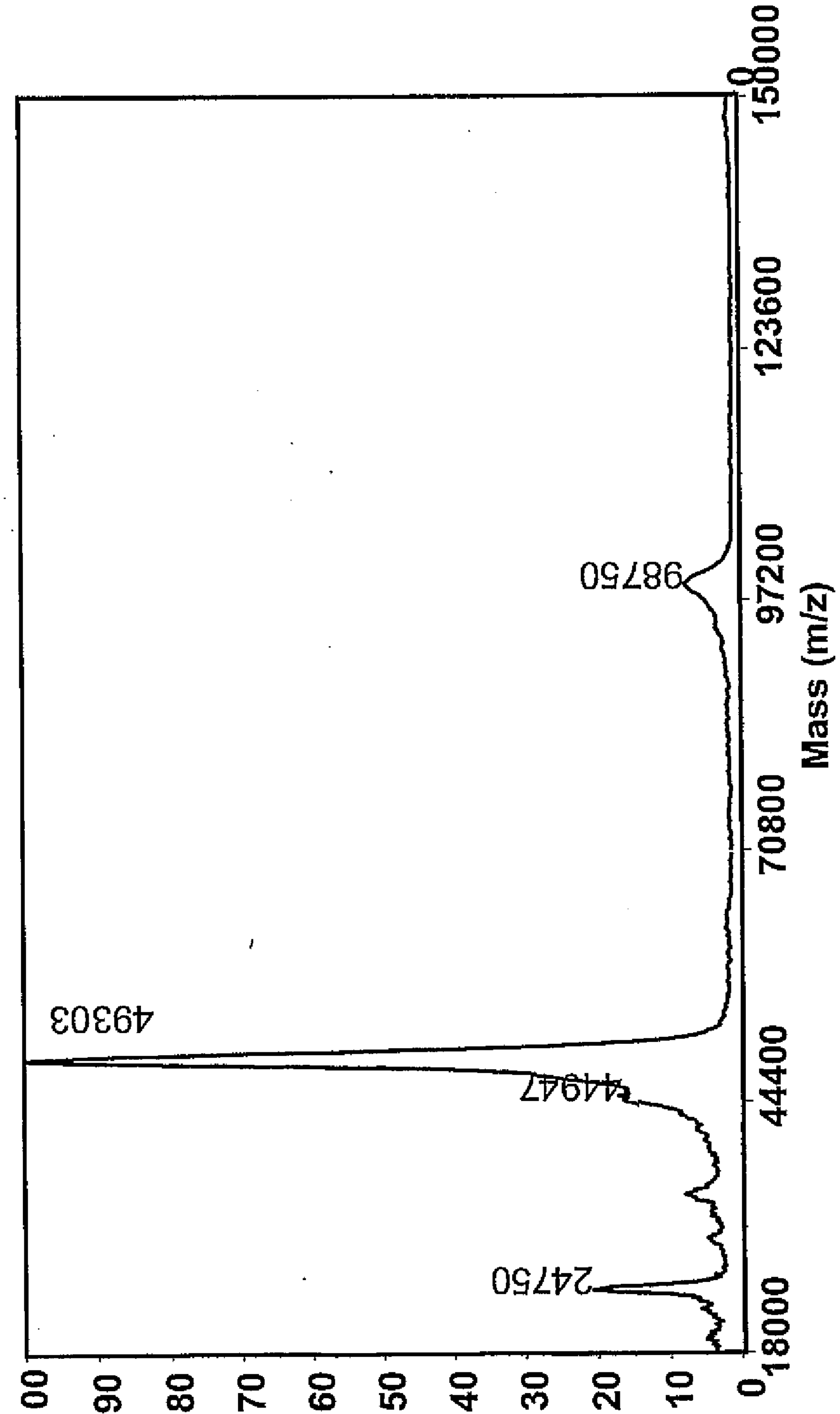

% Intensity
100
90
80
70
60
50
40
30
20
10
0
18000
44400
70800
97200
123600
150000
Mass (m/z)
24750
44947
49303
98750

FIG. 117

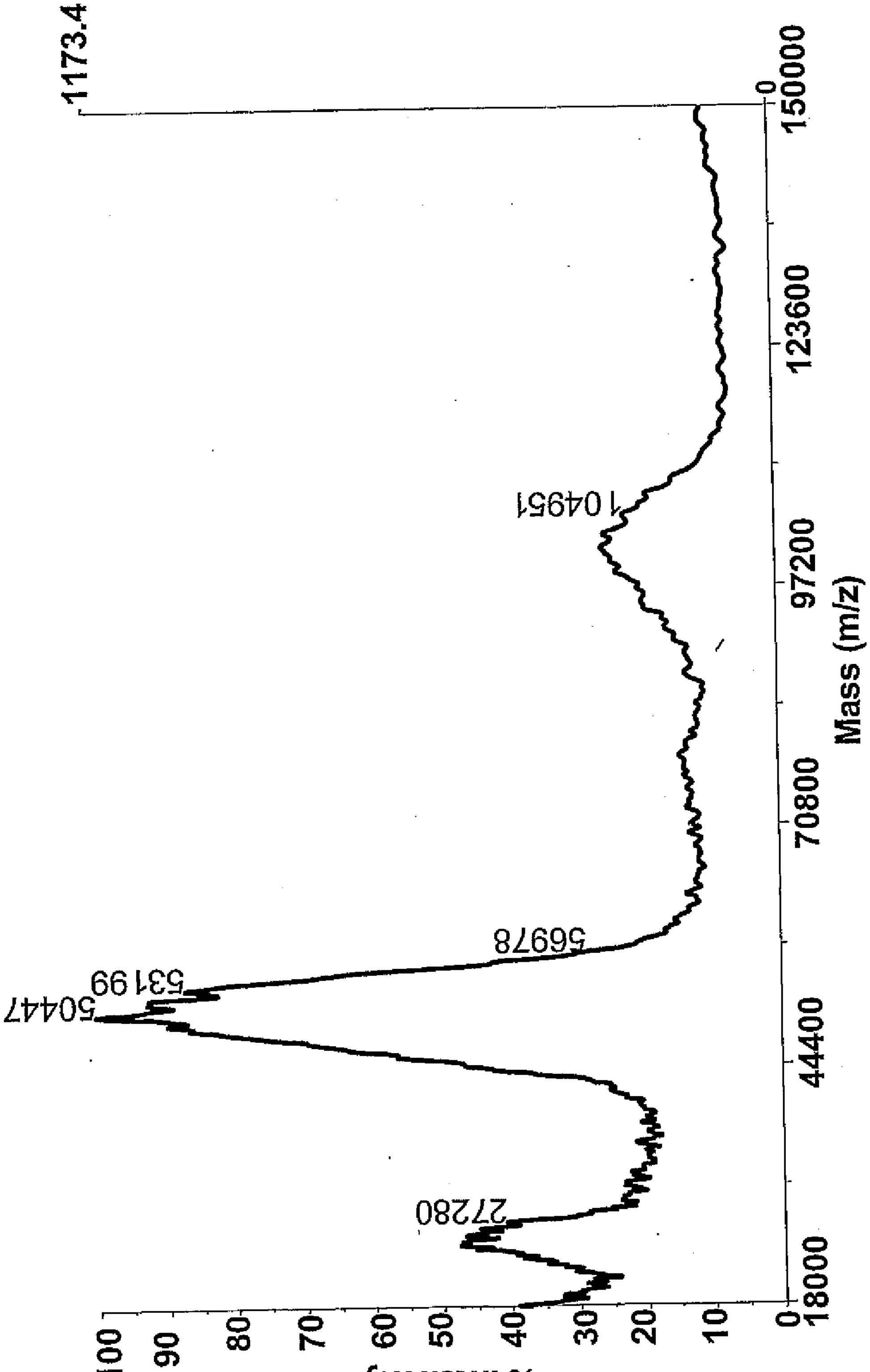

1173.4
0
10
20
30
40
50
60
70
80
90
100
% Intensity
18000
44400
70800
97200
123600
150000
Mass (m/z)
27280
50447
53199
56978
104951

FIG. 118

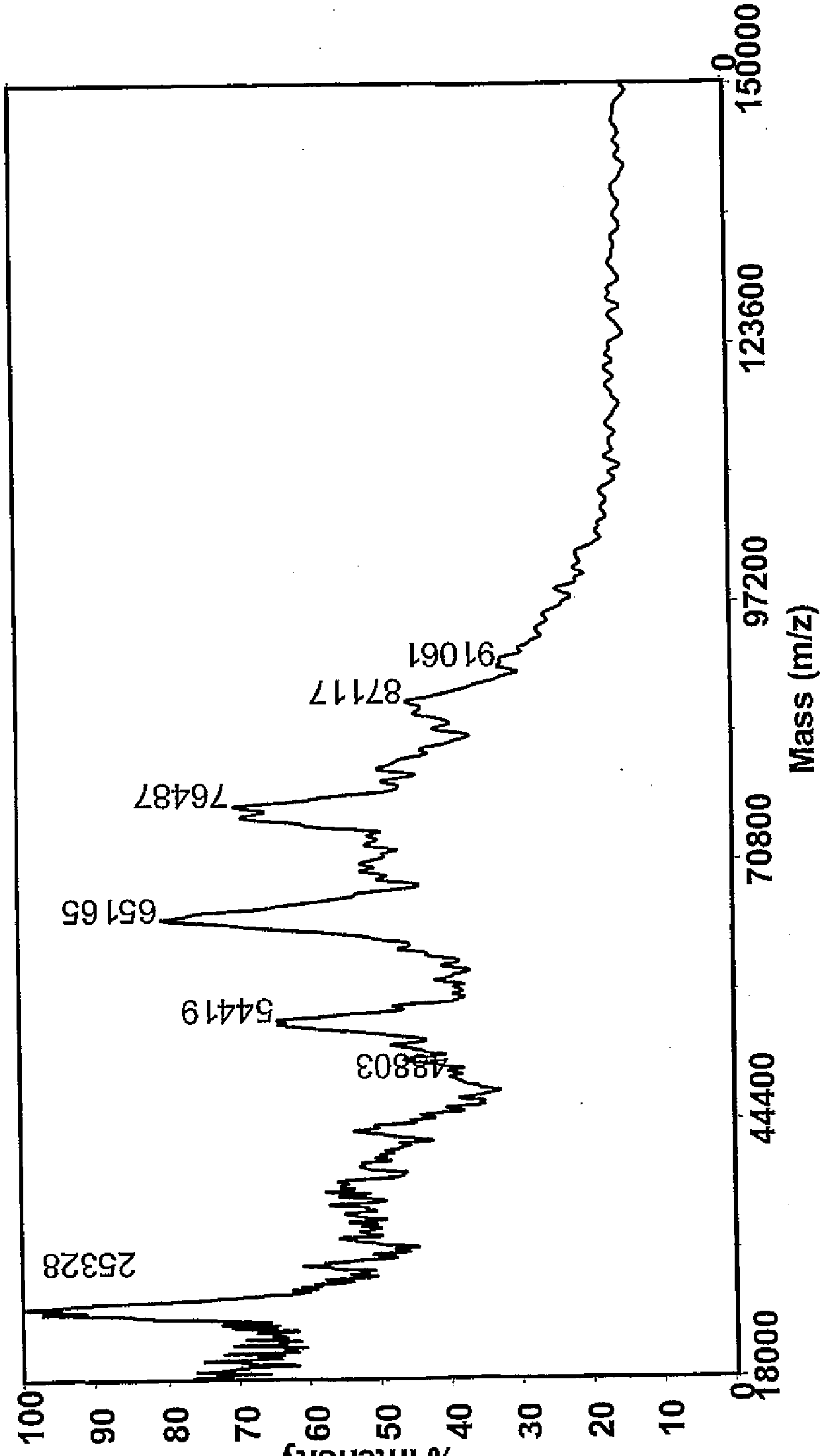

% Intensity
100
90
80
70
60
50
40
30
20
10
0
0
Mass (m/z)
18000
44400
70800
97200
123600
150000
25328
48803
54419
65165
76487
87117
91061

FIG. 119

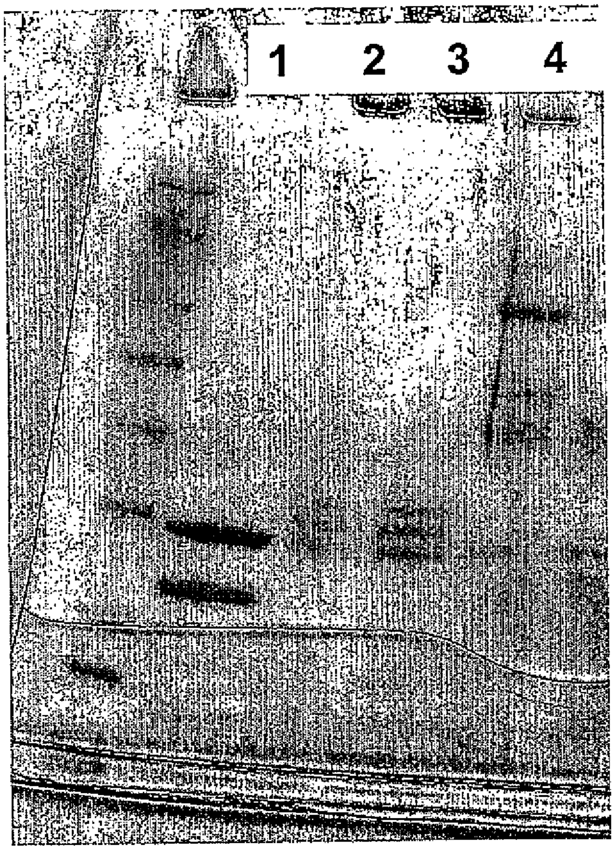


FIG. 120

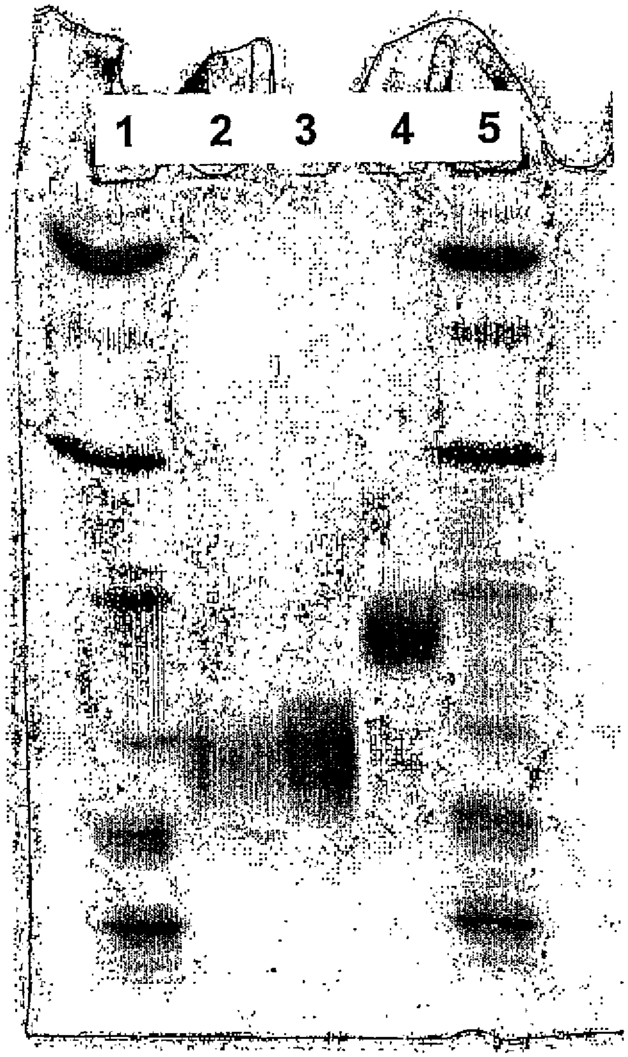


FIG. 121

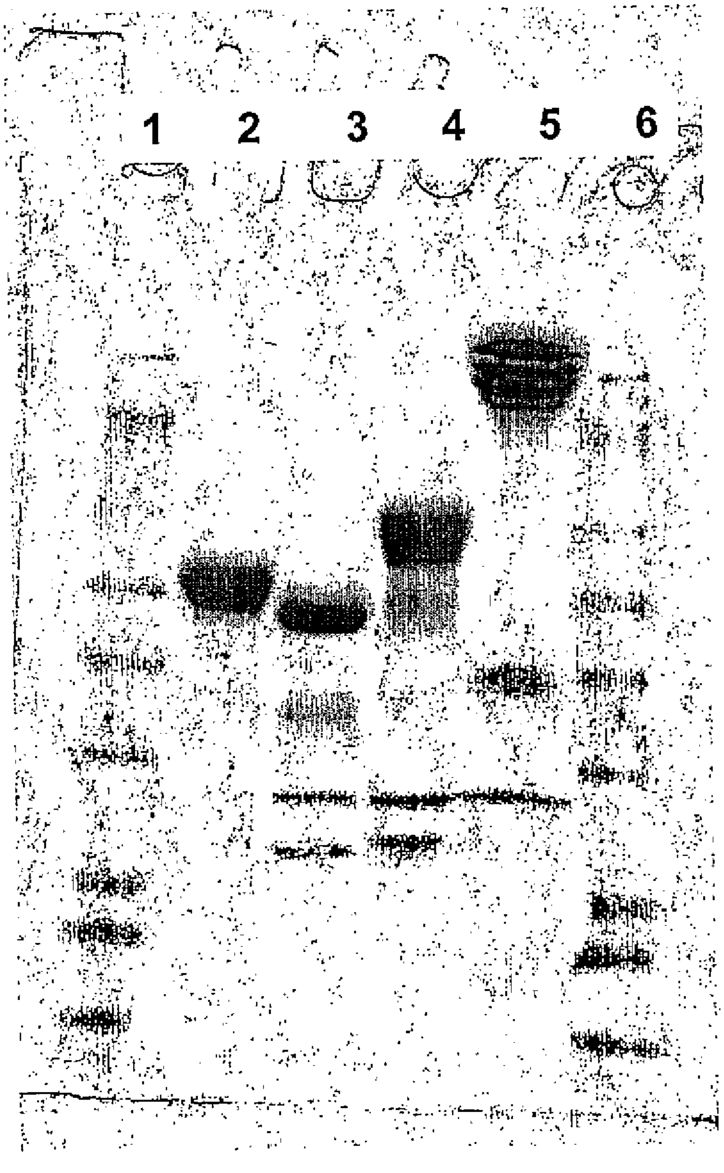


FIG. 122

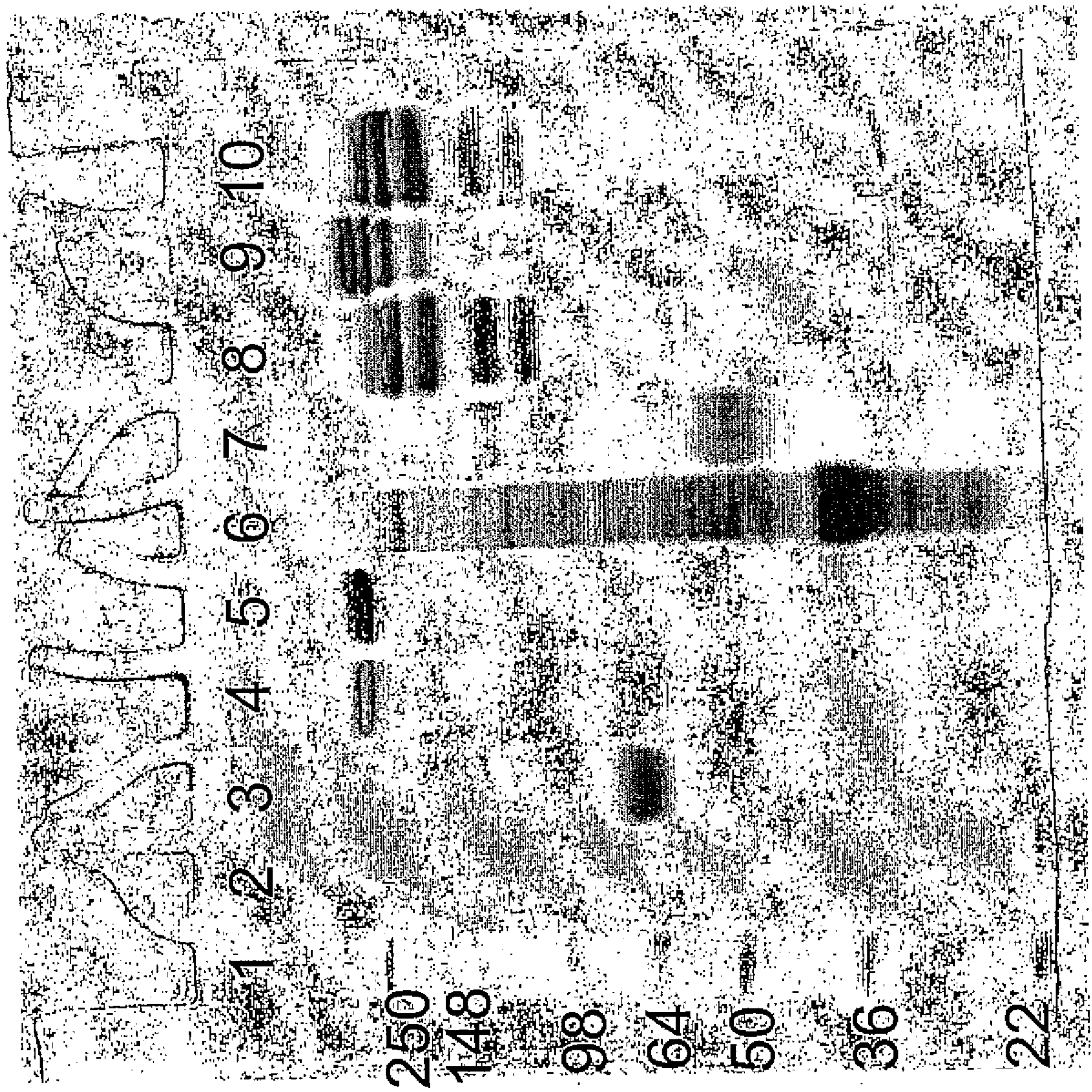


FIG. 123

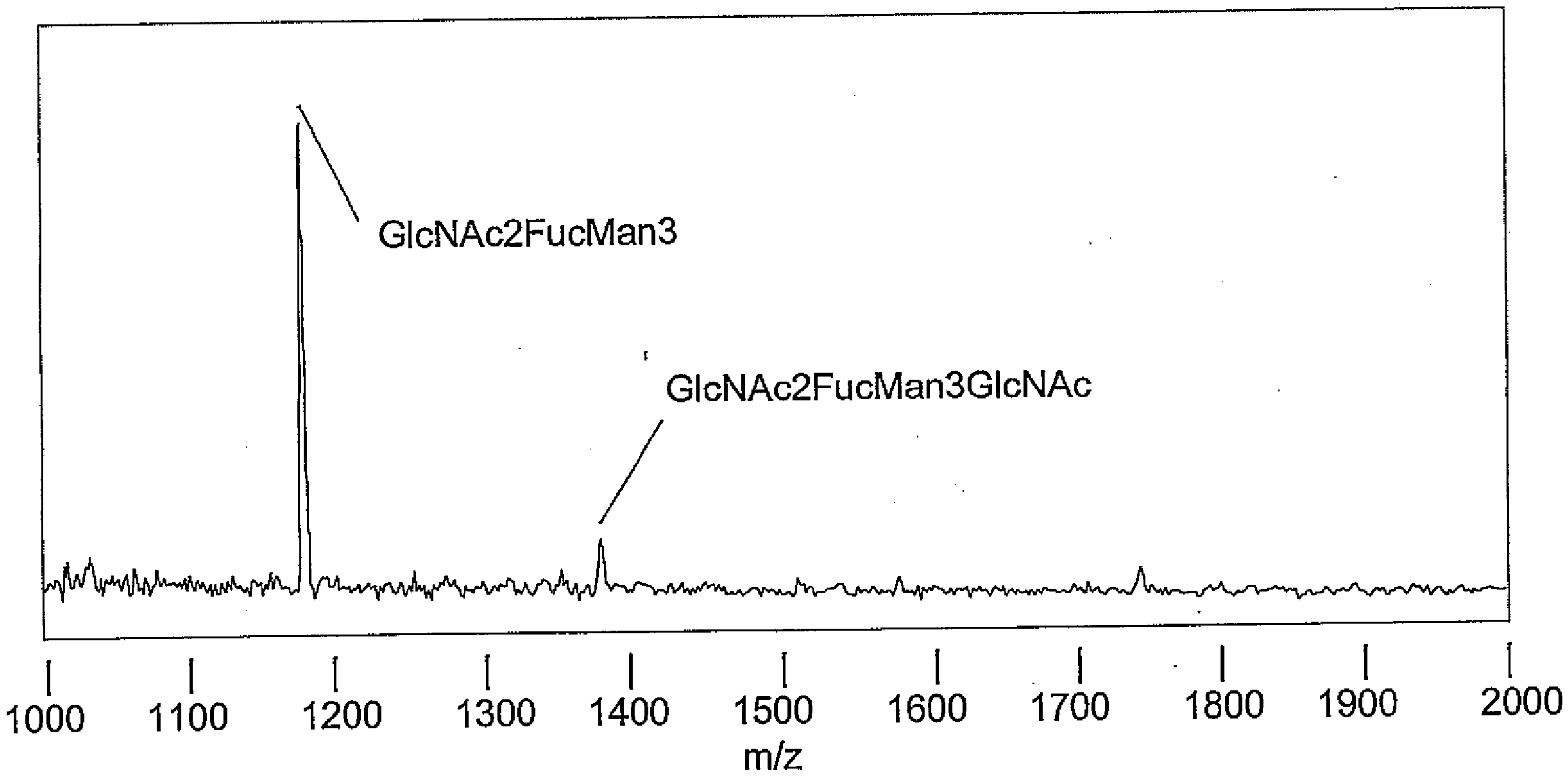

GlcNAc2FucMan3
GlcNAc2FucMan3GlcNAc
1000
1100
1200
1300
1400
1500
1600
1700
1800
1900
2000
m/z

FIG. 124

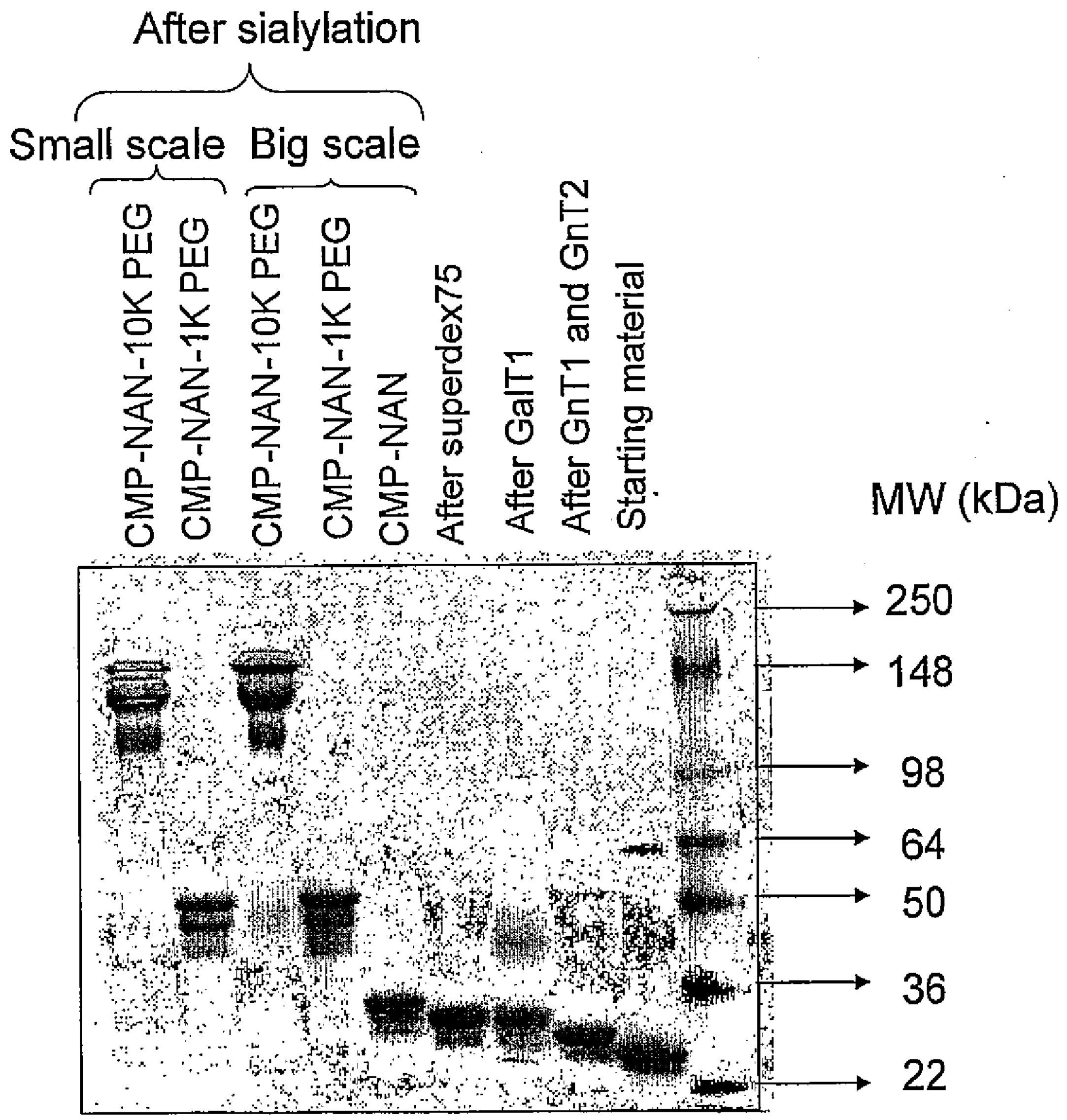

After sialylation
Small scale
Big scale
CMP-NAN-10K PEG
CMP-NAN-1K PEG
CMP-NAN-10K PEG
CMP-NAN-1K PEG
CMP-NAN
After superdex75
After GalT1
After GnT1 and GnT2
Starting material
MW (kDa)
250
148
98
64
50
36
22

FIG. 125

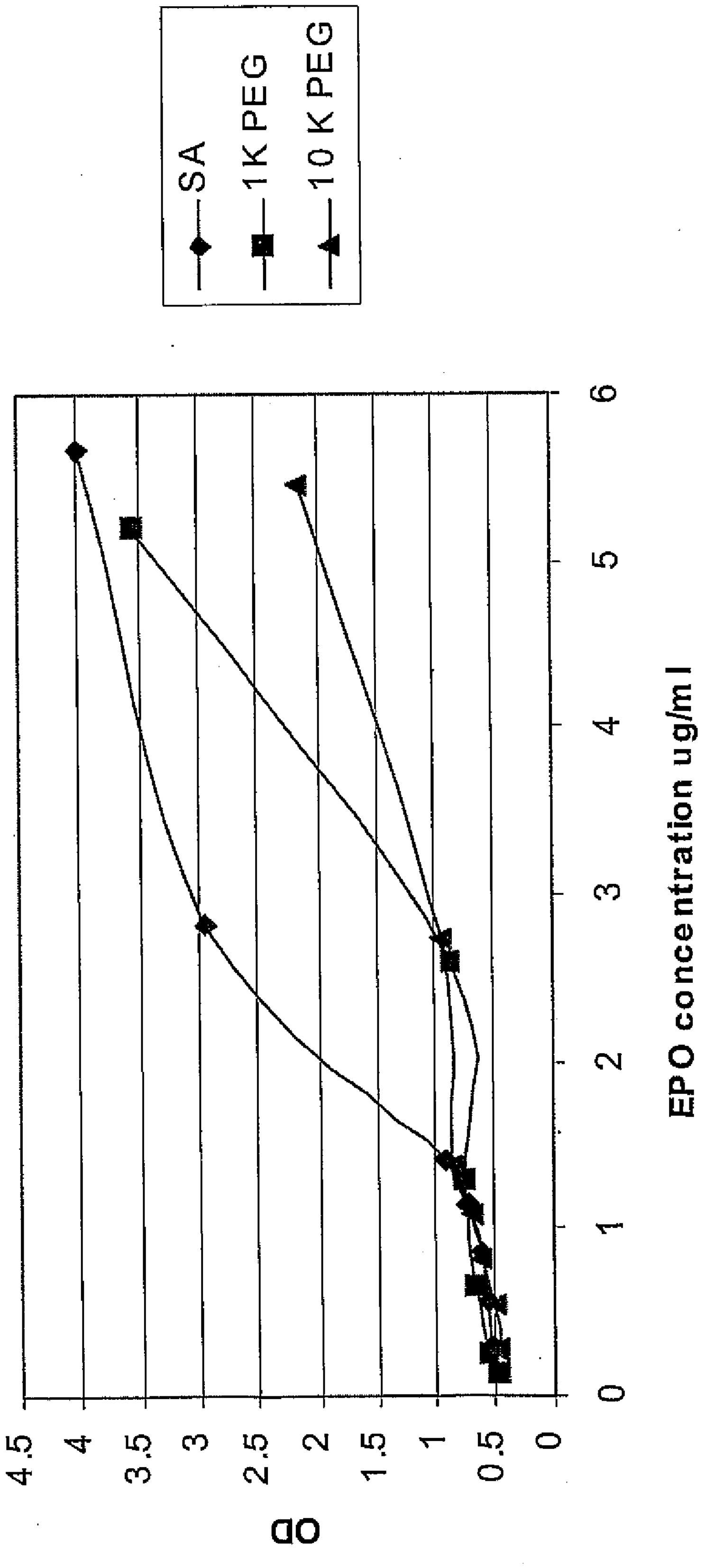

SA
1 K PEG
10 K PEG
OD
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
0
1
2
3
4
5
6
EPO concentration ug/ml

FIG. 126

SEQUENCE LISTING

<110> Neose Technologies, Inc.
DeFrees, Shawn
Zopf, David
Bayer, Robert
Bowe, Caryn
Hakes, David
Chen, Xi

<120> REMODELING AND GLYCOCONJUGATION OF PEPTIDES

<130> 040853-01-5050WO

<150> US 60/328,523
<151> 2001-10-10

<150> US 60/344,692
<151> 2001-10-19

<150> US 60/334,233
<151> 2001-11-08

<150> US 60/334,301
<151> 2001-11-08

<150> US 60/387,292
<151> 2002-06-07

<150> US 60/391,777
<151> 2002-06-25

<150> US 60/396,594
<151> 2002-07-17

<150> US 60/404,249
<151> 2002-08-16

<150> US 60/407,527
<151> 2002-08-28

<160> 62

<170> PatentIn version 3.1

<210> 1
<211> 525
<212> DNA
<213> Homo sapiens

<400> 1
acccccctgg gccctgccag ctccctgccc cagagcttcc tgctcaagtg cttagagcaa 60

gtgaggaaga tccagggcga tggcgcagcg ctccaggaga agctgtgtgc cacctacaag 120

ctgtgccacc ccgaggagct ggtgctgctc ggacactctc tgggcatccc ctgggctccc 180 ctgagcagct gccccagcca ggccctgcag ctggcaggct gcttgagcca actccatagc 240

ggcctttcc tctaccaggg gctcctgcag gccctggaag ggatctcccc cgagttgggt 300

cccaccttgg acacactgca gctggacgtc gccgactttg ccaccaccat ctggcagcag 360

atggaagaac tgggaatggc ccctgccctg cagcccaccc agggtgccat gccggccttc 420

gcctctgctt tccagcgccg ggcaggaggg gtcctggttg cctcccatct gcagagcttc 480

ctggaggtgt cgtaccgcgt tctacgccac cttgcccagc cctga 525

<210> 2
<211> 174
<212> PRT
<213> Homo sapiens

<400> 2

Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys
1 5 10 15

Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln
20 25 30

Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val
35 40 45

Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys
50 55 60

Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser
65 70 75 80

Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser
85 90 95

Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp
100 105 110

Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro
115 120 125

Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe
130 135 140

Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe

145 150 155 160

Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170

<210> 3
<211> 1733
<212> DNA
<213> Homo sapiens

<400> 3
gcgcctctta tgtacccaca aaaatctatt ttcaaaaaag ttgctctaag aatatagtta 60

tcaagttaag taaaatgtca atagcctttt aatttaattt ttaattgttt tatcattctt 120

tgcaataata aaacattaac tttatacttt ttaatttaat gtatagaata gagatataca 180

taggatatgt aaatagatac acagtgtata tgtgattaaa atataatggg agattcaatc 240

agaaaaaagt ttctaaaaag gctctggggt aaaagaggaa ggaaacaata atgaaaaaaa 300

tgtggtgaga aaaacagctg aaaacccatg taaagagtgt ataaagaaag caaaaagaga 360

agtagaaagt aacacagggg catttggaaa atgtaaacga gtatgttccc tatttaaggc 420

taggcacaaa gcaaggtctt cagagaacct ggagcctaag gtttaggctc acccatttca 480

accagtctag cagcatctgc aacatctaca atggccttga cctttgcttt actggtggcc 540

ctcctggtgc tcagctgcaa gtcaagctgc tctgtgggct gtgatctgcc tcaaacccac 600

agcctgggta gcaggaggac cttgatgctc ctggcacaga tgaggagaat ctctcttttc 660

tcctgcttga aggacagaca tgactttgga tttccccagg aggagtttgg caaccagttc 720

caaaaggctg aaaccatccc tgtcctccat gagatgatcc agcagatctt caatctcttc 780

agcacaaagg actcatctgc tgcttgggat gagaccctcc tagacaaatt ctacactgaa 840

ctctaccagc agctgaatga cctggaagcc tgtgtgatac agggggtggg ggtgacagag 900

actcccctga tgaaggagga ctccattctg gctgtgagga aatacttcca aagaatcact 960

ctctatctga aagagaagaa atacagccct tgtgcctggg aggttgtcag agcagaaatc 1020

atgagatctt tttctttgtc aacaaacttg caagaaagtt taagaagtaa ggaatgaaaa 1080

ctggttcaac atggaaatga ttttcattga ttcgtatgcc agctcacctt tttatgatct 1140

gccatttcaa agactcatgt ttctgctatg accatgacac gatttaaatc ttttcaaatg 1200

tttttaggag tattaatcaa cattgtattc agctcttaag gcactagtcc cttacagagg 1260

accatgctga ctgatccatt atctatttaa atatttttaa aatattattt atttaactat 1320 ttataaaaca acttattttt gttcatatta tgtcatgtgc acctttgcac agtggttaat 1380

gtaataaaat gtgttctttg tatttggtaa atttattttg tgttgttcat tgaacttttg 1440

ctatggaact tttgtacttg tttattcttt aaaatgaaat tccaagccta attgtgcaac 1500

ctgattacag aataactggt acacttcatt tgtccatcaa tattatattc aagatataag 1560

taaaaataaa ctttctgtaa accaagttgt atgttgtact caagataaca gggtgaacct 1620

aacaaataca attctgctct cttgtgtatt tgatttttgt atgaaaaaaa ctaaaaatgg 1680

taatcatact taattatcag ttatggtaaa tggtatgaag agaagaagga acg 1733

<210> 4
<211> 188
<212> PRT
<213> Homo sapiens

<400> 4

Met Ala Leu Thr Phe Ala Leu Leu Val Ala Leu Leu Val Leu Ser Cys
1 5 10 15

Lys Ser Ser Cys Ser Val Gly Cys Asp Leu Pro Gln Thr His Ser Leu
20 25 30

Gly Ser Arg Arg Thr Leu Met Leu Leu Ala Gln Met Arg Arg Ile Ser
35 40 45

Leu Phe Ser Cys Leu Lys Asp Arg His Asp Phe Gly Phe Pro Gln Glu
50 55 60

Glu Phe Gly Asn Gln Phe Gln Lys Ala Glu Thr Ile Pro Val Leu His
65 70 75 80

Glu Met Ile Gln Gln Ile Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser
85 90 95

Ala Ala Trp Asp Glu Thr Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr
100 105 110

Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Ile Gln Gly Val Gly Val
115 120 125

Thr Glu Thr Pro Leu Met Lys Glu Asp Ser Ile Leu Ala Val Arg Lys
130 135 140

Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro
145 150 155 160

Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser Leu
165 170 175

Ser Thr Asn Leu Gln Glu Ser Leu Arg Ser Lys Glu
180 185

<210> 5
<211> 757
<212> DNA
<213> Homo sapiens

<400> 5
atgaccaaca agtgtctcct ccaaattgct ctcctgttgt gcttctccac tacagctctt 60

tccatgagct acaacttgct tggattccta caaagaagca gcaattttca gtgtcagaag 120

ctcctgtggc aattgaatgg gaggcttgaa tattgcctca aggacaggat gaactttgac 180

atccctgagg agattaagca gctgcagcag ttccagaagg aggacgccgc attgaccatc 240

tatgagatgc tccagaacat ctttgctatt ttcagacaag attcatctag cactggctgg 300

aatgagacta ttgttgagaa cctcctggct aatgtctatc atcagataaa ccatctgaag 360

acagtcctgg aagaaaaact ggagaaagaa gattttacca ggggaaaact catgagcagt 420

ctgcacctga aaagatatta tgggaggatt ctgcattacc tgaaggccaa ggagtacagt 480

cactgtgcct ggaccatagt cagagtggaa atcctaagga acttttactt cattaacaga 540

cttacaggtt acctccgaaa ctgaagatct cctagcctgt ccctctggga ctggacaatt 600

gcttcaagca ttcttcaacc agcagatgct gtttaagtga ctgatggcta atgtactgca 660

aatgaaagga cactagaaga ttttgaaatt tttattaaat tatgagttat ttttatttat 720

ttaaatttta ttttggaaaa taaattattt ttggtgc 757

<210> 6
<211> 187
<212> PRT
<213> Homo sapiens

<400> 6

Met Thr Asn Lys Cys Leu Leu Gln Ile Ala Leu Leu Leu Cys Phe Ser
1 5 10 15

```
Thr Thr Ala Leu Ser Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg
            20                  25                  30

Ser Ser Asn Phe Gln Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg
        35                  40                  45

Leu Glu Tyr Cys Leu Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu
    50                  55                  60

Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile
65                  70                  75                  80

Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser
                85                  90                  95

Ser Thr Gly Trp Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val
            100                 105                 110

Tyr His Gln Ile Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu
        115                 120                 125

Lys Glu Asp Phe Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys
    130                 135                 140

Arg Tyr Tyr Gly Arg Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser
145                 150                 155                 160

His Cys Ala Trp Thr Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr
                165                 170                 175

Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg Asn
            180                 185


<210>  7
<211>  1332
<212>  DNA
<213>  Homo sapiens

<400>  7
atggtctccc aggccctcag gctcctctgc cttctgcttg ggcttcaggg ctgcctggct      60

gcagtcttcg taacccagga ggaagcccac ggcgtcctgc accggcgccg gcgcgccaac     120

gcgttcctgg aggagctgcg gccgggctcc ctggagaggg agtgcaagga ggagcagtgc     180

tccttcgagg aggcccggga gatcttcaag gacgcggaga ggacgaagct gttctggatt     240
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tcttacagtg atggggacca gtgtgcctca agtccatgcc agaatggggg ctcctgcaag 300

gaccagctcc agtcctatat ctgcttctgc ctccctgcct tcgagggccg gaactgtgag 360

acgcacaagg atgaccagct gatctgtgtg aacgagaacg gcggctgtga gcagtactgc 420

agtgaccaca cgggcaccaa gcgctcctgt cggtgccacg aggggtactc tctgctggca 480

gacggggtgt cctgcacacc cacagttgaa tatccatgtg gaaaaatacc tattctagaa 540

aaaagaaatg ccagcaaacc ccaaggccga attgtggggg gcaaggtgtg ccccaaaggg 600

gagtgtccat ggcaggtcct gttgttggtg aatggagctc agttgtgtgg ggggaccctg 660

atcaacacca tctgggtggt ctccgcggcc cactgtttcg acaaaatcaa gaactggagg 720

aacctgatcg cggtgctggg cgagcacgac ctcagcgagc acgacgggga tgagcagagc 780

cggcgggtgg cgcaggtcat catccccagc acgtacgtcc cgggcaccac caaccacgac 840

atcgcgctgc tccgcctgca ccagcccgtg gtcctcactg accatgtggt gcccctctgc 900

ctgcccgaac ggacgttctc tgagaggacg ctggccttcg tgcgcttctc attggtcagc 960

ggctggggcc agctgctgga ccgtggcgcc acggccctgg agctcatggt gctcaacgtg 1020

ccccggctga tgacccagga ctgcctgcag cagtcacgga aggtgggaga ctccccaaat 1080

atcacggagt acatgttctg tgccggctac tcggatggca gcaaggactc ctgcaagggg 1140

gacagtggag gcccacatgc cacccactac cggggcacgt ggtacctgac gggcatcgtc 1200

agctggggcc agggctgcgc aaccgtgggc cactttgggg tgtacaccag ggtctcccag 1260

tacatcgagt ggctgcaaaa gctcatgcgc tcagagccac gcccaggagt cctcctgcga 1320

gccccatttc cc 1332

<210> 8
<211> 444
<212> PRT
<213> Homo sapiens

<400> 8

Met Val Ser Gln Ala Leu Arg Leu Leu Cys Leu Leu Leu Gly Leu Gln
1 5 10 15

Gly Cys Leu Ala Ala Val Phe Val Thr Gln Glu Glu Ala His Gly Val
20 25 30

Leu His Arg Arg Arg Arg Ala Asn Ala Phe Leu Glu Glu Leu Arg Pro
35 40 45

```
Gly Ser Leu Glu Arg Glu Cys Lys Glu Glu Gln Cys Ser Phe Glu Glu
    50                  55                  60

Ala Arg Glu Ile Phe Lys Asp Ala Glu Arg Thr Lys Leu Phe Trp Ile
65                  70                  75                  80

Ser Tyr Ser Asp Gly Asp Gln Cys Ala Ser Ser Pro Cys Gln Asn Gly
                85                  90                  95

Gly Ser Cys Lys Asp Gln Leu Gln Ser Tyr Ile Cys Phe Cys Leu Pro
            100                 105                 110

Ala Phe Glu Gly Arg Asn Cys Glu Thr His Lys Asp Asp Gln Leu Ile
        115                 120                 125

Cys Val Asn Glu Asn Gly Gly Cys Glu Gln Tyr Cys Ser Asp His Thr
    130                 135                 140

Gly Thr Lys Arg Ser Cys Arg Cys His Glu Gly Tyr Ser Leu Leu Ala
145                 150                 155                 160

Asp Gly Val Ser Cys Thr Pro Thr Val Glu Tyr Pro Cys Gly Lys Ile
                165                 170                 175

Pro Ile Leu Glu Lys Arg Asn Ala Ser Lys Pro Gln Gly Arg Ile Val
            180                 185                 190

Gly Gly Lys Val Cys Pro Lys Gly Glu Cys Pro Trp Gln Val Leu Leu
        195                 200                 205

Leu Val Asn Gly Ala Gln Leu Cys Gly Gly Thr Leu Ile Asn Thr Ile
    210                 215                 220

Trp Val Val Ser Ala Ala His Cys Phe Asp Lys Ile Lys Asn Trp Arg
225                 230                 235                 240

Asn Leu Ile Ala Val Leu Gly Glu His Asp Leu Ser Glu His Asp Gly
                245                 250                 255

Asp Glu Gln Ser Arg Arg Val Ala Gln Val Ile Ile Pro Ser Thr Tyr
            260                 265                 270
```

Val Pro Gly Thr Thr Asn His Asp Ile Ala Leu Leu Arg Leu His Gln
275 280 285

Pro Val Val Leu Thr Asp His Val Val Pro Leu Cys Leu Pro Glu Arg
290 295 300

Thr Phe Ser Glu Arg Thr Leu Ala Phe Val Arg Phe Ser Leu Val Ser
305 310 315 320

Gly Trp Gly Gln Leu Leu Asp Arg Gly Ala Thr Ala Leu Glu Leu Met
325 330 335

Val Leu Asn Val Pro Arg Leu Met Thr Gln Asp Cys Leu Gln Gln Ser
340 345 350

Arg Lys Val Gly Asp Ser Pro Asn Ile Thr Glu Tyr Met Phe Cys Ala
355 360 365

Gly Tyr Ser Asp Gly Ser Lys Asp Ser Cys Lys Gly Asp Ser Gly Gly
370 375 380

Pro His Ala Thr His Tyr Arg Gly Thr Trp Tyr Leu Thr Gly Ile Val
385 390 395 400

Ser Trp Gly Gln Gly Cys Ala Thr Val Gly His Phe Gly Val Tyr Thr
405 410 415

Arg Val Ser Gln Tyr Ile Glu Trp Leu Gln Lys Leu Met Arg Ser Glu
420 425 430

Pro Arg Pro Gly Val Leu Leu Arg Ala Pro Phe Pro
435 440

<210> 9
<211> 1437
<212> DNA
<213> Homo sapiens

<400> 9
atgcagcgcg tgaacatgat catggcagaa tcaccaagcc tcatcaccat ctgcctttta 60

ggatatctac tcagtgctga atgtacagtt tttcttgatc atgaaaacgc caacaaaatt 120

ctgaatcggc caaagaggta taattcaggt aaattggaag agtttgttca agggaacctt 180 gagagagaat gtatggaaga aaagtgtagt tttgaagaac cacgagaagt ttttgaaaac 240

actgaaaaga caactgaatt ttggaagcag tatgttgatg gagatcagtg tgagtccaat 300

ccatgtttaa atggcggcag ttgcaaggat gacattaatt cctatgaatg ttggtgtccc 360

tttggatttg aaggaaagaa ctgtgaatta gatgtaacat gtaacattaa gaatggcaga 420

tgcgagcagt tttgtaaaaa tagtgctgat aacaaggtgg tttgctcctg tactgaggga 480

tatcgacttg cagaaaacca gaagtcctgt gaaccagcag tgccatttcc atgtggaaga 540

gtttctgttt cacaaacttc taagctcacc cgtgctgagg ctgtttttcc tgatgtggac 600

tatgtaaatc ctactgaagc tgaaaccatt ttggataaca tcactcaagg cacccaatca 660

tttaatgact tcactcgggt tgttggtgga gaagatgcca aaccaggtca attcccttgg 720

caggttgttt tgaatggtaa agttgatgca ttctgtggag gctctatcgt taatgaaaaa 780

tggattgtaa ctgctgccca ctgtgttgaa actggtgtta aaattacagt tgtcgcaggt 840

gaacataata ttgaggagac agaacataca gagcaaaagc gaaatgtgat tcgagcaatt 900

attcctcacc acaactacaa tgcagctatt aataagtaca accatgacat tgcccttctg 960

gaactggacg aacccttagt gctaaacagc tacgttacac ctatttgcat tgctgacaag 1020

gaatacacga acatcttcct caaatttgga tctggctatg taagtggctg ggcaagagtc 1080

ttccacaaag ggagatcagc tttagttctt cagtacctta gagttccact tgttgaccga 1140

gccacatgtc ttcgatctac aaagttcacc atctataaca acatgttctg tgctggcttc 1200

catgaaggag gtagagattc atgtcaagga gatagtgggg gaccccatgt tactgaagtg 1260

gaagggacca gtttcttaac tggaattatt agctggggtg aagagtgtgc aatgaaaggc 1320

aaatatggaa tatataccaa ggtatcccgg tatgtcaact ggattaagga aaaaacaaag 1380

ctcacttaat gaaagatgga tttccaaggt taattcattg gaattgaaaa ttaacag 1437

<210> 10
<211> 462
<212> PRT
<213> Homo sapiens

<400> 10

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Ser Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

```
Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
        35                  40                  45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Pro Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Lys Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190

Glu Ala Val Phe Pro Asp Val Asp Tyr Val Asn Pro Thr Glu Ala Glu
        195                 200                 205

Thr Ile Leu Asp Asn Ile Thr Gln Gly Thr Gln Ser Phe Asn Asp Phe
    210                 215                 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225                 230                 235                 240

Gln Val Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile
                245                 250                 255
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Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
            260                 265                 270

Val Lys Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu
        275                 280                 285

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ala Ile Ile Pro His His
    290                 295                 300

Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu
305                 310                 315                 320

Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys
                325                 330                 335

Ile Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly
            340                 345                 350

Tyr Val Ser Gly Trp Ala Arg Val Phe His Lys Gly Arg Ser Ala Leu
        355                 360                 365

Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu
    370                 375                 380

Arg Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe
385                 390                 395                 400

His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His
                405                 410                 415

Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp
            420                 425                 430

Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val
        435                 440                 445

Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr
    450                 455                 460
```

<210> 11
<211> 603
<212> DNA
<213> Homo sapiens

<400> 11
atggattact acagaaaata tgcagctatc tttctggtca cattgtcggt gtttctgcat 60

gttctccatt ccgctcctga tgtgcaggat tgcccagaat gcacgctaca ggaaaaccca 120

ttcttctccc agccgggtgc cccaatactt cagtgcatgg gctgctgctt ctctagagca 180

tatcccactc cactaaggtc caagaagacg atgttggtcc aaaagaacgt cacctcagag 240

tccacttgct gtgtagctaa atcatataac agggtcacag taatgggggg tttcaaagtg 300

gagaaccaca cggcgtgcca ctgcagtact tgttattatc acaaatctta aatgttttac 360

caagtgctgt cttgatgact gctgattttc tggaatggaa aattaagttg tttagtgttt 420

atggctttgt gagataaaac tctccttttc cttaccatac cactttgaca cgcttcaagg 480

atatactgca gctttactgc cttcctcctt atcctacagt acaatcagca gtctagttct 540

tttcatttgg aatgaataca gcattaagct tgttccactg caaataaagc cttttaaatc 600

atc 603

<210> 12
<211> 116
<212> PRT
<213> Homo sapiens

<400> 12

Met Asp Tyr Tyr Arg Lys Tyr Ala Ala Ile Phe Leu Val Thr Leu Ser
1 5 10 15

Val Phe Leu His Val Leu His Ser Ala Pro Asp Val Gln Asp Cys Pro
20 25 30

Glu Cys Thr Leu Gln Glu Asn Pro Phe Phe Ser Gln Pro Gly Ala Pro
35 40 45

Ile Leu Gln Cys Met Gly Cys Cys Phe Ser Arg Ala Tyr Pro Thr Pro
50 55 60

Leu Arg Ser Lys Lys Thr Met Leu Val Gln Lys Asn Val Thr Ser Glu
65 70 75 80

Ser Thr Cys Cys Val Ala Lys Ser Tyr Asn Arg Val Thr Val Met Gly
85 90 95

Gly Phe Lys Val Glu Asn His Thr Ala Cys His Cys Ser Thr Cys Tyr
100 105 110

```
Tyr His Lys Ser
        115


<210>  13
<211>  390
<212>  DNA
<213>  Homo sapiens

<400>  13
atgaagacac tccagttttt cttccttttc tgttgctgga aagcaatctg ctgcaatagc      60

tgtgagctga ccaacatcac cattgcaata gagaaagaag aatgtcgttt ctgcataagc     120

atcaacacca cttggtgtgc tggctactgc tacaccaggg atctggtgta taaggaccca     180

gccaggccca aaatccagaa aacatgtacc ttcaaggaac tggtatatga aacagtgaga     240

gtgcccggct gtgctcacca tgcagattcc ttgtatacat acccagtggc cacccagtgt     300

cactgtggca agtgtgacag cgacagcact gattgtactg tgcgaggcct ggggcccagc     360

tactgctcct ttggtgaaat gaaagaataa                                      390


<210>  14
<211>  129
<212>  PRT
<213>  Homo sapiens

<400>  14

Met Lys Thr Leu Gln Phe Phe Phe Leu Phe Cys Cys Trp Lys Ala Ile
1               5                   10                  15


Cys Cys Asn Ser Cys Glu Leu Thr Asn Ile Thr Ile Ala Ile Glu Lys
            20                  25                  30


Glu Glu Cys Arg Phe Cys Ile Ser Ile Asn Thr Thr Trp Cys Ala Gly
        35                  40                  45


Tyr Cys Tyr Thr Arg Asp Leu Val Tyr Lys Asp Pro Ala Arg Pro Lys
    50                  55                  60


Ile Gln Lys Thr Cys Thr Phe Lys Glu Leu Val Tyr Glu Thr Val Arg
65                  70                  75                  80


Val Pro Gly Cys Ala His His Ala Asp Ser Leu Tyr Thr Tyr Pro Val
                85                  90                  95
```

Ala Thr Gln Cys His Cys Gly Lys Cys Asp Ser Asp Ser Thr Asp Cys
100 105 110

Thr Val Arg Gly Leu Gly Pro Ser Tyr Cys Ser Phe Gly Glu Met Lys
115 120 125

Glu

<210> 15
<211> 1342
<212> DNA
<213> Homo sapiens

<400> 15
cccggagccg gaccggggcc accgcgcccg ctctgctccg acaccgcgcc ccctggacag 60

ccgccctctc ctccaggccc gtggggctgg ccctgcaccg ccgagcttcc cgggatgagg 120

gcccccggtg tggtcacccg gcgcgcccca ggtcgctgag ggaccccggc caggcgcgga 180

gatgggggtg cacgaatgtc ctgcctggct gtggcttctc ctgtccctgc tgtcgctccc 240

tctgggcctc ccagtcctgg gcgccccacc acgcctcatc tgtgacagcc gagtcctgga 300

gaggtacctc ttggaggcca aggaggccga gaatatcacg acgggctgtg ctgaacactg 360

cagcttgaat gagaatatca ctgtcccaga caccaaagtt aatttctatg cctggaagag 420

gatggaggtc gggcagcagg ccgtagaagt ctggcagggc ctggccctgc tgtcggaagc 480

tgtcctgcgg ggccaggccc tgttggtcaa ctcttcccag ccgtgggagc ccctgcagct 540

gcatgtggat aaagccgtca gtggccttcg cagcctcacc actctgcttc gggctctgcg 600

agcccagaag gaagccatct cccctccaga tgcggcctca gctgctccac tccgaacaat 660

cactgctgac actttccgca aactcttccg agtctactcc aatttcctcc ggggaaagct 720

gaagctgtac acaggggagg cctgcaggac aggggacaga tgaccaggtg tgtccacctg 780

ggcatatcca ccacctccct caccaacatt gcttgtgcca caccctcccc cgccactcct 840

gaaccccgtc gaggggctct cagctcagcg ccagcctgtc ccatggacac tccagtgcca 900

gcaatgacat ctcaggggcc agaggaactg tccagagagc aactctgaga tctaaggatg 960

tcacagggcc aacttgaggg cccagagcag gaagcattca gagagcagct ttaaactcag 1020

ggacagagcc atgctgggaa gacgcctgag ctcactcggc accctgcaaa atttgatgcc 1080

aggacacgct ttggaggcga tttacctgtt ttcgcaccta ccatcaggga caggatgacc 1140

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tggagaactt aggtggcaag ctgtgacttc tccaggtctc acgggcatgg gcactcccct    1200

ggtggcaaga gcccccttga caccggggtg gtgggaacca tgaagacagg atgggggctg    1260

gcctctggct ctcatggggt ccaagttttg tgtattcttc aacctcattg acaagaactg    1320

aaaccaccaa aaaaaaaaaa aa                                             1342


<210>  16
<211>  193
<212>  PRT
<213>  Homo sapiens

<400>  16

Met Gly Val His Glu Cys Pro Ala Trp Leu Trp Leu Leu Leu Ser Leu
1               5                   10                  15


Leu Ser Leu Pro Leu Gly Leu Pro Val Leu Gly Ala Pro Pro Arg Leu
            20                  25                  30


Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Lys Glu
        35                  40                  45


Ala Glu Asn Ile Thr Thr Gly Cys Ala Glu His Cys Ser Leu Asn Glu
    50                  55                  60


Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe Tyr Ala Trp Lys Arg
65                  70                  75                  80


Met Glu Val Gly Gln Gln Ala Val Glu Val Trp Gln Gly Leu Ala Leu
                85                  90                  95


Leu Ser Glu Ala Val Leu Arg Gly Gln Ala Leu Leu Val Asn Ser Ser
            100                 105                 110


Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp Lys Ala Val Ser Gly
        115                 120                 125


Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu Arg Ala Gln Lys Glu
    130                 135                 140


Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile
145                 150                 155                 160


Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu
```

165 170 175

Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala Cys Arg Thr Gly Asp
180 185 190

Arg

<210> 17
<211> 435
<212> DNA
<213> Homo sapiens

<400> 17
atgtggctgc agagcctgct gctcttgggc actgtggcct gcagcatctc tgcacccgcc 60

cgctcgccca gccccagcac gcagccctgg gagcatgtga atgccatcca ggaggcccgg 120

cgtctcctga acctgagtag agacactgct gctgagatga atgaaacagt agaagtcatc 180

tcagaaatgt ttgacctcca ggagccgacc tgcctacaga cccgcctgga gctgtacaag 240

cagggcctgc ggggcagcct caccaagctc aagggcccct tgaccatgat ggccagccac 300

tacaagcagc actgccctcc aaccccggaa acttcctgtg caacccagat tatcaccttt 360

gaaagtttca aagagaacct gaaggacttt ctgcttgtca tcccctttga ctgctgggag 420

ccagtccagg agtga 435

<210> 18
<211> 144
<212> PRT
<213> Homo sapiens

<400> 18

Met Trp Leu Gln Ser Leu Leu Leu Leu Gly Thr Val Ala Cys Ser Ile
1 5 10 15

Ser Ala Pro Ala Arg Ser Pro Ser Pro Ser Thr Gln Pro Trp Glu His
20 25 30

Val Asn Ala Ile Gln Glu Ala Arg Arg Leu Leu Asn Leu Ser Arg Asp
35 40 45

Thr Ala Ala Glu Met Asn Glu Thr Val Glu Val Ile Ser Glu Met Phe
50 55 60

Asp Leu Gln Glu Pro Thr Cys Leu Gln Thr Arg Leu Glu Leu Tyr Lys
65 70 75 80

Gln Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro Leu Thr Met
85 90 95

Met Ala Ser His Tyr Lys Gln His Cys Pro Pro Thr Pro Glu Thr Ser
100 105 110

Cys Ala Thr Gln Ile Ile Thr Phe Glu Ser Phe Lys Glu Asn Leu Lys
115 120 125

Asp Phe Leu Leu Val Ile Pro Phe Asp Cys Trp Glu Pro Val Gln Glu
130 135 140

<210> 19
<211> 501
<212> DNA
<213> Homo sapiens

<400> 19
atgaaatata caagttatat cttggctttt cagctctgca tcgttttggg ttctcttggc 60

tgttactgcc aggacccata tgtaaaagaa gcagaaaacc ttaagaaata ttttaatgca 120

ggtcattcag atgtagcgga taatggaact cttttcttag gcattttgaa gaattggaaa 180

gaggagagtg acagaaaaat aatgcagagc caaattgtct ccttttactt caaacttttt 240

aaaaacttta aagatgacca gagcatccaa aagagtgtgg agaccatcaa ggaagacatg 300

aatgtcaagt ttttcaatag caacaaaaag aaacgagatg acttcgaaaa gctgactaat 360

tattcggtaa ctgacttgaa tgtccaacgc aaagcaatac atgaactcat ccaagtgatg 420

gctgaactgt cgccagcagc taaaacaggg aagcgaaaaa ggagtcagat gctgtttcga 480

ggtcgaagag catcccagta a 501

<210> 20
<211> 166
<212> PRT
<213> Homo sapiens

<400> 20

Met Lys Tyr Thr Ser Tyr Ile Leu Ala Phe Gln Leu Cys Ile Val Leu
1 5 10 15

Gly Ser Leu Gly Cys Tyr Cys Gln Asp Pro Tyr Val Lys Glu Ala Glu

```
            20                  25                  30

Asn Leu Lys Lys Tyr Phe Asn Ala Gly His Ser Asp Val Ala Asp Asn
        35                  40                  45

Gly Thr Leu Phe Leu Gly Ile Leu Lys Asn Trp Lys Glu Glu Ser Asp
    50                  55                  60

Arg Lys Ile Met Gln Ser Gln Ile Val Ser Phe Tyr Phe Lys Leu Phe
65                  70                  75                  80

Lys Asn Phe Lys Asp Asp Gln Ser Ile Gln Lys Ser Val Glu Thr Ile
                85                  90                  95

Lys Glu Asp Met Asn Val Lys Phe Phe Asn Ser Asn Lys Lys Lys Arg
            100                 105                 110

Asp Asp Phe Glu Lys Leu Thr Asn Tyr Ser Val Thr Asp Leu Asn Val
        115                 120                 125

Gln Arg Lys Ala Ile His Glu Leu Ile Gln Val Met Ala Glu Leu Ser
    130                 135                 140

Pro Ala Ala Lys Thr Gly Lys Arg Lys Arg Ser Gln Met Leu Phe Arg
145                 150                 155                 160

Gly Arg Arg Ala Ser Gln
                165


<210>  21
<211>  1352
<212>  DNA
<213>  Homo sapiens

<400>  21
ctgggacagt gaatcgacaa tgccgtcttc tgtctcgtgg ggcatcctcc tgctggcagg      60

cctgtgctgc ctggtccctg tctccctggc tgaggatccc cagggagatg ctgcccagaa     120

gacagataca tcccaccatg atcaggatca cccaaccttc aacaagatca cccccaacct     180

ggctgagttc gccttcagcc tataccgcca gctggcacac cagtccaaca gcaccaatat     240

cttcttctcc ccagtgagca tcgctacagc ctttgcaatg ctctccctgg ggaccaaggc     300

tgacactcac gatgaaatcc tggagggcct gaatttcaac ctcacggaga ttccggaggc     360
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tcagatccat gaaggcttcc aggaactcct ccgtaccctc aaccagccag acagccagct     420

ccagctgacc accggcaatg gcctgttcct cagcgagggc ctgaagctag tggataagtt     480

tttggaggat gttaaaaagt tgtaccactc agaagccttc actgtcaact tcggggacac     540

cgaagaggcc aagaaacaga tcaacgatta cgtggagaag ggtactcaag ggaaaattgt     600

ggatttggtc aaggagcttg acagagacac agtttttgct ctggtgaatt acatcttctt     660

taaaggcaaa tgggagagac cctttgaagt caaggacacc gaggaagagg acttccacgt     720

ggaccaggtg accaccgtga aggtgcctat gatgaagcgt ttaggcatgt ttaacatcca     780

gcactgtaag aagctgtcca gctgggtgct gctgatgaaa tacctgggca atgccaccgc     840

catcttcttc ctgcctgatg aggggaaact acagcacctg gaaaatgaac tcacccacga     900

tatcatcacc aagttcctgg aaaatgaaga cagaaggtct gccagcttac atttacccaa     960

actgtccatt actggaacct atgatctgaa gagcgtcctg ggtcaactgg gcatcactaa    1020

ggtcttcagc aatggggctg acctctccgg ggtcacagag gaggcacccc tgaagctctc    1080

caaggccgtg cataaggctg tgctgaccat cgacgagaaa gggactgaag ctgctggggc    1140

catgttttta gaggccatac ccatgtctat cccccccgag gtcaagttca acaaaccctt    1200

tgtcttctta atgattgaac aaaataccaa gtctcccctc ttcatgggaa aagtggtgaa    1260

tcccacccaa aaataactgc ctctcgctcc tcaacccctc ccctccatcc ctggcccccct   1320

ccctggatga cattaaagaa gggttgagct gg                                  1352


<210>  22
<211>  418
<212>  PRT
<213>  Homo sapiens

<400>  22

Met Pro Ser Ser Val Ser Trp Gly Ile Leu Leu Leu Ala Gly Leu Cys
1               5                   10                  15


Cys Leu Val Pro Val Ser Leu Ala Glu Asp Pro Gln Gly Asp Ala Ala
            20                  25                  30


Gln Lys Thr Asp Thr Ser His His Asp Gln Asp His Pro Thr Phe Asn
        35                  40                  45


Lys Ile Thr Pro Asn Leu Ala Glu Phe Ala Phe Ser Leu Tyr Arg Gln
    50                  55                  60
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Leu Ala His Gln Ser Asn Ser Thr Asn Ile Phe Phe Ser Pro Val Ser
65 70 75 80

Ile Ala Thr Ala Phe Ala Met Leu Ser Leu Gly Thr Lys Ala Asp Thr
85 90 95

His Asp Glu Ile Leu Glu Gly Leu Asn Phe Asn Leu Thr Glu Ile Pro
100 105 110

Glu Ala Gln Ile His Glu Gly Phe Gln Glu Leu Leu Arg Thr Leu Asn
115 120 125

Gln Pro Asp Ser Gln Leu Gln Leu Thr Thr Gly Asn Gly Leu Phe Leu
130 135 140

Ser Glu Gly Leu Lys Leu Val Asp Lys Phe Leu Glu Asp Val Lys Lys
145 150 155 160

Leu Tyr His Ser Glu Ala Phe Thr Val Asn Phe Gly Asp Thr Glu Glu
165 170 175

Ala Lys Lys Gln Ile Asn Asp Tyr Val Glu Lys Gly Thr Gln Gly Lys
180 185 190

Ile Val Asp Leu Val Lys Glu Leu Asp Arg Asp Thr Val Phe Ala Leu
195 200 205

Val Asn Tyr Ile Phe Phe Lys Gly Lys Trp Glu Arg Pro Phe Glu Val
210 215 220

Lys Asp Thr Glu Glu Glu Asp Phe His Val Asp Gln Val Thr Thr Val
225 230 235 240

Lys Val Pro Met Met Lys Arg Leu Gly Met Phe Asn Ile Gln His Cys
245 250 255

Lys Lys Leu Ser Ser Trp Val Leu Leu Met Lys Tyr Leu Gly Asn Ala
260 265 270

Thr Ala Ile Phe Phe Leu Pro Asp Glu Gly Lys Leu Gln His Leu Glu
275 280 285

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Asn Glu Leu Thr His Asp Ile Ile Thr Lys Phe Leu Glu Asn Glu Asp
    290                 295                 300


Arg Arg Ser Ala Ser Leu His Leu Pro Lys Leu Ser Ile Thr Gly Thr
305                 310                 315                 320


Tyr Asp Leu Lys Ser Val Leu Gly Gln Leu Gly Ile Thr Lys Val Phe
                325                 330                 335


Ser Asn Gly Ala Asp Leu Ser Gly Val Thr Glu Glu Ala Pro Leu Lys
            340                 345                 350


Leu Ser Lys Ala Val His Lys Ala Val Leu Thr Ile Asp Glu Lys Gly
        355                 360                 365


Thr Glu Ala Ala Gly Ala Met Phe Leu Glu Ala Ile Pro Met Ser Ile
    370                 375                 380


Pro Pro Glu Val Lys Phe Asn Lys Pro Phe Val Phe Leu Met Ile Glu
385                 390                 395                 400


Gln Asn Thr Lys Ser Pro Leu Phe Met Gly Lys Val Val Asn Pro Thr
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Gln Lys


<210>  23
<211>  2004
<212>  DNA
<213>  Homo sapiens

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ggatggagtt ttcaagtcct tccagagagg aatgtcccaa gcctttgagt agggtaagca     180

tcatggctgg cagcctcaca ggtttgcttc tacttcaggc agtgtcgtgg gcatcaggtg     240

cccgcccctg catccctaaa agcttcggct acagctcggt ggtgtgtgtc tgcaatgcca     300

catactgtga ctcctttgac cccccgacct ttcctgccct tggtaccttc agccgctatg     360

agagtacacg cagtgggcga cggatggagc tgagtatggg gcccatccag gctaatcaca     420

cgggcacagg cctgctactg accctgcagc cagaacagaa gttccagaaa gtgaagggat     480
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tacccatggc cagctgtgac ttctccatcc gcacctacac ctatgcagac acccctgatg     660
atttccagtt gcacaacttc agcctcccag aggaagatac caagctcaag atacccctga     720
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ggggcaatgg tttgggtgac tcactttccc ctctaggtgg tgcccagggc tggaggcccc    1920
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<210> 24
<211> 536
<212> PRT

<213> Homo sapiens

<400> 24

Met Glu Phe Ser Ser Pro Ser Arg Glu Glu Cys Pro Lys Pro Leu Ser
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Arg Val Ser Ile Met Ala Gly Ser Leu Thr Gly Leu Leu Leu Leu Gln
20 25 30

Ala Val Ser Trp Ala Ser Gly Ala Arg Pro Cys Ile Pro Lys Ser Phe
35 40 45

Gly Tyr Ser Ser Val Val Cys Val Cys Asn Ala Thr Tyr Cys Asp Ser
50 55 60

Phe Asp Pro Pro Thr Phe Pro Ala Leu Gly Thr Phe Ser Arg Tyr Glu
65 70 75 80

Ser Thr Arg Ser Gly Arg Arg Met Glu Leu Ser Met Gly Pro Ile Gln
85 90 95

Ala Asn His Thr Gly Thr Gly Leu Leu Leu Thr Leu Gln Pro Glu Gln
100 105 110

Lys Phe Gln Lys Val Lys Gly Phe Gly Gly Ala Met Thr Asp Ala Ala
115 120 125

Ala Leu Asn Ile Leu Ala Leu Ser Pro Pro Ala Gln Asn Leu Leu Leu
130 135 140

Lys Ser Tyr Phe Ser Glu Glu Gly Ile Gly Tyr Asn Ile Ile Arg Val
145 150 155 160

Pro Met Ala Ser Cys Asp Phe Ser Ile Arg Thr Tyr Thr Tyr Ala Asp
165 170 175

Thr Pro Asp Asp Phe Gln Leu His Asn Phe Ser Leu Pro Glu Glu Asp
180 185 190

Thr Lys Leu Lys Ile Pro Leu Ile His Arg Ala Leu Gln Leu Ala Gln
195 200 205

Arg Pro Val Ser Leu Leu Ala Ser Pro Trp Thr Ser Pro Thr Trp Leu

210 215 220

Lys Thr Asn Gly Ala Val Asn Gly Lys Gly Ser Leu Lys Gly Gln Pro
225 230 235 240

Gly Asp Ile Tyr His Gln Thr Trp Ala Arg Tyr Phe Val Lys Phe Leu
245 250 255

Asp Ala Tyr Ala Glu His Lys Leu Gln Phe Trp Ala Val Thr Ala Glu
260 265 270

Asn Glu Pro Ser Ala Gly Leu Leu Ser Gly Tyr Pro Phe Gln Cys Leu
275 280 285

Gly Phe Thr Pro Glu His Gln Arg Asp Phe Ile Ala Arg Asp Leu Gly
290 295 300

Pro Thr Leu Ala Asn Ser Thr His His Asn Val Arg Leu Leu Met Leu
305 310 315 320

Asp Asp Gln Arg Leu Leu Leu Pro His Trp Ala Lys Val Val Leu Thr
325 330 335

Asp Pro Glu Ala Ala Lys Tyr Val His Gly Ile Ala Val His Trp Tyr
340 345 350

Leu Asp Phe Leu Ala Pro Ala Lys Ala Thr Leu Gly Glu Thr His Arg
355 360 365

Leu Phe Pro Asn Thr Met Leu Phe Ala Ser Glu Ala Cys Val Gly Ser
370 375 380

Lys Phe Trp Glu Gln Ser Val Arg Leu Gly Ser Trp Asp Arg Gly Met
385 390 395 400

Gln Tyr Ser His Ser Ile Ile Thr Asn Leu Leu Tyr His Val Val Gly
405 410 415

Trp Thr Asp Trp Asn Leu Ala Leu Asn Pro Glu Gly Gly Pro Asn Trp
420 425 430

Val Arg Asn Phe Val Asp Ser Pro Ile Ile Val Asp Ile Thr Lys Asp
435 440 445

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Thr Phe Tyr Lys Gln Pro Met Phe Tyr His Leu Gly His Phe Ser Lys
    450                 455                 460

Phe Ile Pro Glu Gly Ser Gln Arg Val Gly Leu Val Ala Ser Gln Lys
465                 470                 475                 480

Asn Asp Leu Asp Ala Val Ala Leu Met His Pro Asp Gly Ser Ala Val
                485                 490                 495

Val Val Val Leu Asn Arg Ser Ser Lys Asp Val Pro Leu Thr Ile Lys
            500                 505                 510

Asp Pro Ala Val Gly Phe Leu Glu Thr Ile Ser Pro Gly Tyr Ser Ile
        515                 520                 525

His Thr Tyr Leu Trp His Arg Gln
    530                 535


<210>  25
<211>  1726
<212>  DNA
<213>  Homo sapiens

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tgcagagatg aaaaaacgca gatgatatac cagcaacatc agtcatggct gcgccctgtg     180

ctcagaagca accgggtgga atattgctgg tgcaacagtg gcagggcaca gtgccactca     240

gtgcctgtca aaagttgcag cgagccaagg tgtttcaacg gggggcacctg ccagcaggcc    300

ctgtacttct cagatttcgt gtgccagtgc cccgaaggat ttgctgggaa gtgctgtgaa     360

atagatacca gggccacgtg ctacgaggac cagggcatca gctacagggg cacgtggagc     420

acagcggaga gtggcgccga gtgcaccaac tggaacagca gcgcgttggc ccagaagccc     480

tacagcgggc ggaggccaga cgccatcagg ctgggcctgg ggaaccacaa ctactgcaga     540

aacccagatc gagactcaaa gccctggtgc tacgtcttta aggcggggaa gtacagctca     600

gagttctgca gcacccctgc ctgctctgag ggaaacagtg actgctactt tgggaatggg     660

tcagcctacc gtggcacgca cagcctcacc gagtcgggtg cctcctgcct cccgtggaat     720

tccatgatcc tgataggcaa ggtttacaca gcacagaacc ccagtgccca ggcactgggc     780
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ctgaagaacc gcaggctgac gtgggagtac tgtgatgtgc cctcctgctc cacctgcggc 900

ctgagacagt acagccagcc tcagtttcgc atcaaaggag ggctcttcgc cgacatcgcc 960

tcccacccct ggcaggctgc catctttgcc aagcacagga ggtcgccggg agagcggttc 1020

ctgtgcgggg gcatactcat cagctcctgc tggattctct ctgccgccca ctgcttccag 1080

gagaggtttc cgccccacca cctgacggtg atcttgggca gaacataccg ggtggtccct 1140

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caggagagca gcgtggtccg cactgtgtgc cttcccccgg cggacctgca gctgccggac 1320

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gagcggctga aggaggctca tgtcagactg tacccatcca gccgctgcac atcacaacat 1440

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aacgatggcc gcatgacttt ggtgggcatc atcagctggg gcctgggctg tggacagaag 1620

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cgaccgtgac caggaacacc cgactcctca aaagcaaatg agatcc 1726

<210> 26
<211> 562
<212> PRT
<213> Homo sapiens

<400> 26

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Ala Val Phe Val Ser Pro Ser Gln Glu Ile His Ala Arg Phe Arg Arg
20 25 30

Gly Ala Arg Ser Tyr Gln Val Ile Cys Arg Asp Glu Lys Thr Gln Met
35 40 45

Ile Tyr Gln Gln His Gln Ser Trp Leu Arg Pro Val Leu Arg Ser Asn
50 55 60

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Arg Val Glu Tyr Cys Trp Cys Asn Ser Gly Arg Ala Gln Cys His Ser
65                  70                  75                  80

Val Pro Val Lys Ser Cys Ser Glu Pro Arg Cys Phe Asn Gly Gly Thr
                85                  90                  95

Cys Gln Gln Ala Leu Tyr Phe Ser Asp Phe Val Cys Gln Cys Pro Glu
            100                 105                 110

Gly Phe Ala Gly Lys Cys Cys Glu Ile Asp Thr Arg Ala Thr Cys Tyr
        115                 120                 125

Glu Asp Gln Gly Ile Ser Tyr Arg Gly Thr Trp Ser Thr Ala Glu Ser
    130                 135                 140

Gly Ala Glu Cys Thr Asn Trp Asn Ser Ser Ala Leu Ala Gln Lys Pro
145                 150                 155                 160

Tyr Ser Gly Arg Arg Pro Asp Ala Ile Arg Leu Gly Leu Gly Asn His
                165                 170                 175

Asn Tyr Cys Arg Asn Pro Asp Arg Asp Ser Lys Pro Trp Cys Tyr Val
            180                 185                 190

Phe Lys Ala Gly Lys Tyr Ser Ser Glu Phe Cys Ser Thr Pro Ala Cys
        195                 200                 205

Ser Glu Gly Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr Arg
    210                 215                 220

Gly Thr His Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn
225                 230                 235                 240

Ser Met Ile Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala
                245                 250                 255

Gln Ala Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly
            260                 265                 270

Asp Ala Lys Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp
        275                 280                 285

Glu Tyr Cys Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr
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    290                 295                 300

Ser Gln Pro Gln Phe Arg Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala
305                 310                 315                 320

Ser His Pro Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro
                325                 330                 335

Gly Glu Arg Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile
            340                 345                 350

Leu Ser Ala Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu
        355                 360                 365

Thr Val Ile Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Glu
    370                 375                 380

Gln Lys Phe Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp
385                 390                 395                 400

Asp Thr Tyr Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser
                405                 410                 415

Ser Arg Cys Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu Pro
            420                 425                 430

Pro Ala Asp Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly
        435                 440                 445

Tyr Gly Lys His Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Lys
    450                 455                 460

Glu Ala His Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His
465                 470                 475                 480

Leu Leu Asn Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp Thr
                485                 490                 495

Arg Ser Gly Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln Gly Asp
            500                 505                 510

Ser Gly Gly Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val
        515                 520                 525
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Gly Ile Ile Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val Pro Gly
530 535 540

Val Tyr Thr Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp Asn Met
545 550 555 560

Arg Pro

<210> 27
<211> 825
<212> DNA
<213> Homo sapiens

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gttcgacaaa gaaaacaaag aaaacacagc tacaactgga gcatttactg ctggatttac 180
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ccagggactt aatcagcaat atcaacgtaa tagttctgga actaaaggga tctgaaacaa 420
cattcatgtg tgaatatgca gatgagacag caaccattgt agaatttctg aacagatgga 480
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aacatatcag gccttctatt tatttattta aatatttaaa ttttatattt attgttgaat 600
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<210> 28
<211> 156
<212> PRT
<213> Homo sapiens

<400> 28

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ile Leu Ala Leu

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Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Lys Lys
20 25 30

Thr Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu
35 40 45

Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr
50 55 60

Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys Gln Leu Gln
65 70 75 80

Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala
85 90 95

Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile
100 105 110

Asn Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys
115 120 125

Glu Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp
130 135 140

Ile Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr
145 150 155

<210> 29
<211> 7931
<212> DNA
<213> Homo sapiens

<400> 29
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ggtgagctgc ctgtggacgc aagatttcct cctagagtgc caaaatcttt tccattcaac 180

acctcagtcg tgtacaaaaa gactctgttt gtagaattca cggatcacct tttcaacatc 240

gctaagccaa ggccaccctg gatgggtctg ctaggtccta ccatccaggc tgaggtttat 300

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gctgcatctg ctcgggcctg gcctaaaatg cacacagtca atggttatgt aaacaggtct 780

ctgccaggtc tgattggatg ccacaggaaa tcagtctatt ggcatgtgat tggaatgggc 840

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cgccaggcgt ccttggaaat ctcgccaata actttcctta ctgctcaaac actcttgatg 960

gaccttggac agtttctact gttttgtcat atctcttccc accaacatga tggcatggaa 1020

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gaagcggaag actatgatga tgatcttact gattctgaaa tggatgtggt caggtttgat 1140

gatgacaact ctccttcctt tatccaaatt cgctcagttg ccaagaagca tcctaaaact 1200

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gatctagctt caggactcat tggccctctc ctcatctgct acaaagaatc tgtagatcaa 1740

agaggaaacc agataatgtc agacaagagg aatgtcatcc tgttttctgt atttgatgag 1800

aaccgaagct ggtacctcac agagaatata caacgctttc tccccaatcc agctggagtg 1860

cagcttgagg atccagagtt ccaagcctcc aacatcatgc acagcatcaa tggctatgtt 1920

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attggagcac agactgactt cctttctgtc ttcttctctg gatatacctt caaacacaaa 2040

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atgaccgcct tactgaaggt ttctagttgt gacaagaaca ctggtgatta ttacgaggac 2220

agttatgaag atatttcagc atacttgctg agtaaaaaca atgccattga accaagaagc 2280

ttctcccaga attcaagaca ccgtagcact aggcaaaagc aatttaatgc caccacaatt 2340

ccagaaaatg acatagagaa gactgaccct tggtttgcac acagaacacc tatgcctaaa 2400

atacaaaatg tctcctctag tgatttgttg atgctcttgc gacagagtcc tactccacat 2460

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aaactgggga caactgcagc aacagagttg aagaaacttg atttcaaagt ttctagtaca 2700

tcaaataatc tgatttcaac aattccatca gacaatttgg cagcaggtac tgataataca 2760

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tttggcaaaa agtcatctcc ccttactgag tctggtggac ctctgagctt gagtgaagaa 2880

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gctttgttga ctaaagataa tgccttattc aaagttagca tctctttgtt aaagacaaac 3060

aaaacttcca ataattcagc aactaataga aagactcaca ttgatggccc atcattatta 3120

attgagaata gtccatcagt ctggcaaaat atattagaaa gtgacactga gtttaaaaaa 3180

gtgacacctt tgattcatga cagaatgctt atggacaaaa atgctacagc tttgaggcta 3240

aatcatatgt caaataaaac tacttcatca aaaaacatgg aaatggtcca acagaaaaaa 3300

gagggcccca ttccaccaga tgcacaaaat ccagatatgt cgttctttaa gatgctattc 3360

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ttacatgaaa ataatacaca caatcaagaa aaaaaaattc aggaagaaat agaaaagaag 3660

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Trp Asp Tyr Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg
35 40 45

Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val
50 55 60

Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile
65 70 75 80

Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln
85 90 95

```
Ala Glu Val Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser
            100                 105                 110

His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser
        115                 120                 125

Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp
    130                 135                 140

Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu
145                 150                 155                 160

Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser
                165                 170                 175

Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile
            180                 185                 190

Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr
        195                 200                 205

Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly
    210                 215                 220

Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp
225                 230                 235                 240

Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr
                245                 250                 255

Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val
            260                 265                 270

Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile
        275                 280                 285

Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser
    290                 295                 300

Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met
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Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His
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Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro
340 345 350

Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp
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Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser
370 375 380

Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr
385 390 395 400

Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro
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Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn
420 425 430

Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met
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Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu
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Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu
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Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro
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His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys
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Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe
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Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp
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Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg

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Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu
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Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val
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Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu
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Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp
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Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val
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Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp
645 650 655

Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe
660 665 670

Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr
675 680 685

Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro
690 695 700

Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly
705 710 715 720

Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp
725 730 735

Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys
740 745 750

Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Ser Arg His Arg
755 760 765

Ser Thr Arg Gln Lys Gln Phe Asn Ala Thr Thr Ile Pro Glu Asn Asp
770 775 780

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Ile Glu Lys Thr Asp Pro Trp Phe Ala His Arg Thr Pro Met Pro Lys
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Ile Gln Asn Val Ser Ser Ser Asp Leu Leu Met Leu Leu Arg Gln Ser
                805                 810                 815

Pro Thr Pro His Gly Leu Ser Leu Ser Asp Leu Gln Glu Ala Lys Tyr
            820                 825                 830

Glu Thr Phe Ser Asp Asp Pro Ser Pro Gly Ala Ile Asp Ser Asn Asn
        835                 840                 845

Ser Leu Ser Glu Met Thr His Phe Arg Pro Gln Leu His His Ser Gly
    850                 855                 860

Asp Met Val Phe Thr Pro Glu Ser Gly Leu Gln Leu Arg Leu Asn Glu
865                 870                 875                 880

Lys Leu Gly Thr Thr Ala Ala Thr Glu Leu Lys Lys Leu Asp Phe Lys
                885                 890                 895

Val Ser Ser Thr Ser Asn Asn Leu Ile Ser Thr Ile Pro Ser Asp Asn
            900                 905                 910

Leu Ala Ala Gly Thr Asp Asn Thr Ser Ser Leu Gly Pro Pro Ser Met
        915                 920                 925

Pro Val His Tyr Asp Ser Gln Leu Asp Thr Thr Leu Phe Gly Lys Lys
    930                 935                 940

Ser Ser Pro Leu Thr Glu Ser Gly Gly Pro Leu Ser Leu Ser Glu Glu
945                 950                 955                 960

Asn Asn Asp Ser Lys Leu Leu Glu Ser Gly Leu Met Asn Ser Gln Glu
                965                 970                 975

Ser Ser Trp Gly Lys Asn Val Ser Ser Thr Glu Ser Gly Arg Leu Phe
            980                 985                 990

Lys Gly Lys Arg Ala His Gly Pro Ala Leu Leu Thr Lys Asp Asn Ala
        995                 1000                1005
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Leu Phe Lys Val Ser Ile Ser Leu Leu Lys Thr Asn Lys Thr Ser
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Asn Asn Ser Ala Thr Asn Arg Lys Thr His Ile Asp Gly Pro Ser
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Leu Leu Ile Glu Asn Ser Pro Ser Val Trp Gln Asn Ile Leu Glu
1040 1045 1050

Ser Asp Thr Glu Phe Lys Lys Val Thr Pro Leu Ile His Asp Arg
1055 1060 1065

Met Leu Met Asp Lys Asn Ala Thr Ala Leu Arg Leu Asn His Met
1070 1075 1080

Ser Asn Lys Thr Thr Ser Ser Lys Asn Met Glu Met Val Gln Gln
1085 1090 1095

Lys Lys Glu Gly Pro Ile Pro Pro Asp Ala Gln Asn Pro Asp Met
1100 1105 1110

Ser Phe Phe Lys Met Leu Phe Leu Pro Glu Ser Ala Arg Trp Ile
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Gln Arg Thr His Gly Lys Asn Ser Leu Asn Ser Gly Gln Gly Pro
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Ser Pro Lys Gln Leu Val Ser Leu Gly Pro Glu Lys Ser Val Glu
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Gly Gln Asn Phe Leu Ser Glu Lys Asn Lys Val Val Val Gly Lys
1160 1165 1170

Gly Glu Phe Thr Lys Asp Val Gly Leu Lys Glu Met Val Phe Pro
1175 1180 1185

Ser Ser Arg Asn Leu Phe Leu Thr Asn Leu Asp Asn Leu His Glu
1190 1195 1200

Asn Asn Thr His Asn Gln Glu Lys Lys Ile Gln Glu Glu Ile Glu
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Lys Lys  Glu Thr Leu Ile Gln  Glu Asn Val Val Leu  Pro Gln Ile
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His Thr  Val Thr Gly Thr Lys  Asn Phe Met Lys Asn  Leu Phe Leu
    1235                 1240                 1245

Leu Ser  Thr Arg Gln Asn Val  Glu Gly Ser Tyr Asp  Gly Ala Tyr
    1250                 1255                 1260

Ala Pro  Val Leu Gln Asp Phe  Arg Ser Leu Asn Asp  Ser Thr Asn
    1265                 1270                 1275

Arg Thr  Lys Lys His Thr Ala  His Phe Ser Lys Lys  Gly Glu Glu
    1280                 1285                 1290

Glu Asn  Leu Glu Gly Leu Gly  Asn Gln Thr Lys Gln  Ile Val Glu
    1295                 1300                 1305

Lys Tyr  Ala Cys Thr Thr Arg  Ile Ser Pro Asn Thr  Ser Gln Gln
    1310                 1315                 1320

Asn Phe  Val Thr Gln Arg Ser  Lys Arg Ala Leu Lys  Gln Phe Arg
    1325                 1330                 1335

Leu Pro  Leu Glu Glu Thr Glu  Leu Glu Lys Arg Ile  Ile Val Asp
    1340                 1345                 1350

Asp Thr  Ser Thr Gln Trp Ser  Lys Asn Met Lys His  Leu Thr Pro
    1355                 1360                 1365

Ser Thr  Leu Thr Gln Ile Asp  Tyr Asn Glu Lys Glu  Lys Gly Ala
    1370                 1375                 1380

Ile Thr  Gln Ser Pro Leu Ser  Asp Cys Leu Thr Arg  Ser His Ser
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Ile Pro  Gln Ala Asn Arg Ser  Pro Leu Pro Ile Ala  Lys Val Ser
    1400                 1405                 1410

Ser Phe  Pro Ser Ile Arg Pro  Ile Tyr Leu Thr Arg  Val Leu Phe
    1415                 1420                 1425

Gln Asp  Asn Ser Ser His Leu  Pro Ala Ala Ser Tyr  Arg Lys Lys
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Asp Ser Gly Val Gln Glu Ser Ser His Phe Leu Gln Gly Ala Lys
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Asp Gln Arg Glu Val Gly Ser Leu Gly Thr Ser Ala Thr Asn Ser
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Val Thr Tyr Lys Lys Val Glu Asn Thr Val Leu Pro Lys Pro Asp
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Leu Pro Lys Thr Ser Gly Lys Val Glu Leu Leu Pro Lys Val His
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Ile Tyr Gln Lys Asp Leu Phe Pro Thr Glu Thr Ser Asn Gly Ser
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Pro Gly His Leu Asp Leu Val Glu Gly Ser Leu Leu Gln Gly Thr
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Glu Gly Ala Ile Lys Trp Asn Glu Ala Asn Arg Pro Gly Lys Val
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Pro Phe Leu Arg Val Ala Thr Glu Ser Ser Ala Lys Thr Pro Ser
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Lys Leu Leu Asp Pro Leu Ala Trp Asp Asn His Tyr Gly Thr Gln
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Ile Pro Lys Glu Glu Trp Lys Ser Gln Glu Lys Ser Pro Glu Lys
1595 1600 1605

Thr Ala Phe Lys Lys Lys Asp Thr Ile Leu Ser Leu Asn Ala Cys
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Glu Ser Asn His Ala Ile Ala Ala Ile Asn Glu Gly Gln Asn Lys
1625 1630 1635

Pro Glu Ile Glu Val Thr Trp Ala Lys Gln Gly Arg Thr Glu Arg
1640 1645 1650

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Leu Cys  Ser Gln Asn Pro Pro  Val Leu Lys Arg His  Gln Arg Glu
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Ile Thr  Arg Thr Thr Leu Gln  Ser Asp Gln Glu Glu  Ile Asp Tyr
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Asp Asp  Thr Ile Ser Val Glu  Met Lys Lys Glu Asp  Phe Asp Ile
    1685                 1690                 1695

Tyr Asp  Glu Asp Glu Asn Gln  Ser Pro Arg Ser Phe  Gln Lys Lys
    1700                 1705                 1710

Thr Arg  His Tyr Phe Ile Ala  Ala Val Glu Arg Leu  Trp Asp Tyr
    1715                 1720                 1725

Gly Met  Ser Ser Ser Pro His  Val Leu Arg Asn Arg  Ala Gln Ser
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Gly Ser  Val Pro Gln Phe Lys  Lys Val Val Phe Gln  Glu Phe Thr
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Asp Gly  Ser Phe Thr Gln Pro  Leu Tyr Arg Gly Glu  Leu Asn Glu
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His Leu  Gly Leu Leu Gly Pro  Tyr Ile Arg Ala Glu  Val Glu Asp
    1775                 1780                 1785

Asn Ile  Met Val Thr Phe Arg  Asn Gln Ala Ser Arg  Pro Tyr Ser
    1790                 1795                 1800

Phe Tyr  Ser Ser Leu Ile Ser  Tyr Glu Glu Asp Gln  Arg Gln Gly
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Ala Glu  Pro Arg Lys Asn Phe  Val Lys Pro Asn Glu  Thr Lys Thr
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Tyr Phe  Trp Lys Val Gln His  His Met Ala Pro Thr  Lys Asp Glu
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Phe Asp  Cys Lys Ala Trp Ala  Tyr Phe Ser Asp Val  Asp Leu Glu
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Lys Asp  Val His Ser Gly Leu  Ile Gly Pro Leu Leu  Val Cys His
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Glu Phe  Ala Leu Phe Phe Thr  Ile Phe Asp Glu Thr  Lys Ser Trp
    1895                1900                1905

Tyr Phe  Thr Glu Asn Met Glu  Arg Asn Cys Arg Ala  Pro Cys Asn
    1910                1915                1920

Ile Gln  Met Glu Asp Pro Thr  Phe Lys Glu Asn Tyr  Arg Phe His
    1925                1930                1935

Ala Ile  Asn Gly Tyr Ile Met  Asp Thr Leu Pro Gly  Leu Val Met
    1940                1945                1950

Ala Gln  Asp Gln Arg Ile Arg  Trp Tyr Leu Leu Ser  Met Gly Ser
    1955                1960                1965

Asn Glu  Asn Ile His Ser Ile  His Phe Ser Gly His  Val Phe Thr
    1970                1975                1980

Val Arg  Lys Lys Glu Glu Tyr  Lys Met Ala Leu Tyr  Asn Leu Tyr
    1985                1990                1995

Pro Gly  Val Phe Glu Thr Val  Glu Met Leu Pro Ser  Lys Ala Gly
    2000                2005                2010

Ile Trp  Arg Val Glu Cys Leu  Ile Gly Glu His Leu  His Ala Gly
    2015                2020                2025

Met Ser  Thr Leu Phe Leu Val  Tyr Ser Asn Lys Cys  Gln Thr Pro
    2030                2035                2040

Leu Gly  Met Ala Ser Gly His  Ile Arg Asp Phe Gln  Ile Thr Ala
    2045                2050                2055

Ser Gly  Gln Tyr Gly Gln Trp  Ala Pro Lys Leu Ala  Arg Leu His
    2060                2065                2070
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Tyr Ser  Gly Ser Ile Asn Ala  Trp Ser Thr Lys Glu  Pro Phe Ser
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Trp Ile  Lys Val Asp Leu Leu  Ala Pro Met Ile Ile  His Gly Ile
    2090                 2095                 2100

Lys Thr  Gln Gly Ala Arg Gln  Lys Phe Ser Ser Leu  Tyr Ile Ser
    2105                 2110                 2115

Gln Phe  Ile Ile Met Tyr Ser  Leu Asp Gly Lys Lys  Trp Gln Thr
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Tyr Arg  Gly Asn Ser Thr Gly  Thr Leu Met Val Phe  Phe Gly Asn
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Val Asp  Ser Ser Gly Ile Lys  His Asn Ile Phe Asn  Pro Pro Ile
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Ile Ala  Arg Tyr Ile Arg Leu  His Pro Thr His Tyr  Ser Ile Arg
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Ser Thr  Leu Arg Met Glu Leu  Met Gly Cys Asp Leu  Asn Ser Cys
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Ser Met  Pro Leu Gly Met Glu  Ser Lys Ala Ile Ser  Asp Ala Gln
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Ile Thr  Ala Ser Ser Tyr Phe  Thr Asn Met Phe Ala  Thr Trp Ser
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Pro Ser  Lys Ala Arg Leu His  Leu Gln Gly Arg Ser  Asn Ala Trp
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Arg Pro  Gln Val Asn Asn Pro  Lys Glu Trp Leu Gln  Val Asp Phe
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Gln Lys  Thr Met Lys Val Thr  Gly Val Thr Thr Gln  Gly Val Lys
    2255                 2260                 2265

Ser Leu  Leu Thr Ser Met Tyr  Val Lys Glu Phe Leu  Ile Ser Ser
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Ser Gln  Asp Gly His Gln Trp  Thr Leu Phe Phe Gln  Asn Gly Lys
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Val Lys Val Phe Gln Gly Asn Gln Asp Ser Phe Thr Pro Val Val
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gcccgggcca gcaccgggag ctcagattct tcccctggtg gccatgggac ccaggtcaat 1140

gtcacctgca tcgtgaacgt ctgtagcagc tctgaccaca gctcacagtg ctcctcccaa 1200

gccagctcca caatgggaga cacagattcc agcccctcgg agtccccgaa ggacgagcag 1260

gtccccttct ccaaggagga atgtgccttt cggtcacagc tggagacgcc agagaccctg 1320

ctggggagca ccgaagagaa gcccctgccc cttggagtgc ctgatgctgg gatgaagccc 1380

agttaaccag gccggtgtgg gctgtgtcgt agccaaggtg ggctgagccc tggcaggatg 1440

accctgcgaa ggggccctgg tccttccagg c 1471

<210> 32
<211> 461
<212> PRT
<213> Homo sapiens

<400> 32

Met Ala Pro Val Ala Val Trp Ala Ala Leu Ala Val Gly Leu Glu Leu
1 5 10 15

Trp Ala Ala Ala His Ala Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr
20 25 30

Ala Pro Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln
35 40 45

Thr Ala Gln Met Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys
50 55 60

Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp
65 70 75 80

Ser Thr Tyr Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys
85 90 95

Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg
100 105 110

Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu
115 120 125

```
Ser Lys Gln Glu Gly Cys Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg
    130                 135                 140

Pro Gly Phe Gly Val Ala Arg Pro Gly Thr Glu Thr Ser Asp Val Val
145                 150                 155                 160

Cys Lys Pro Cys Ala Pro Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr
                165                 170                 175

Asp Ile Cys Arg Pro His Gln Ile Cys Asn Val Val Ala Ile Pro Gly
            180                 185                 190

Asn Ala Ser Met Asp Ala Val Cys Thr Ser Thr Ser Pro Thr Arg Ser
        195                 200                 205

Met Ala Pro Gly Ala Val His Leu Pro Gln Pro Val Ser Thr Arg Ser
    210                 215                 220

Gln His Thr Gln Pro Thr Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser
225                 230                 235                 240

Phe Leu Leu Pro Met Gly Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly
                245                 250                 255

Asp Phe Ala Leu Pro Val Gly Leu Ile Val Gly Val Thr Ala Leu Gly
            260                 265                 270

Leu Leu Ile Ile Gly Val Val Asn Cys Val Ile Met Thr Gln Val Lys
        275                 280                 285

Lys Lys Pro Leu Cys Leu Gln Arg Glu Ala Lys Val Pro His Leu Pro
    290                 295                 300

Ala Asp Lys Ala Arg Gly Thr Gln Gly Pro Glu Gln Gln His Leu Leu
305                 310                 315                 320

Ile Thr Ala Pro Ser Ser Ser Ser Ser Ser Leu Glu Ser Ser Ala Ser
                325                 330                 335

Ala Leu Asp Arg Arg Ala Pro Thr Arg Asn Gln Pro Gln Ala Pro Gly
            340                 345                 350
```

Val Glu Ala Ser Gly Ala Gly Glu Ala Arg Ala Ser Thr Gly Ser Ser
355 360 365

Asp Ser Ser Pro Gly Gly His Gly Thr Gln Val Asn Val Thr Cys Ile
370 375 380

Val Asn Val Cys Ser Ser Ser Asp His Ser Ser Gln Cys Ser Ser Gln
385 390 395 400

Ala Ser Ser Thr Met Gly Asp Thr Asp Ser Ser Pro Ser Glu Ser Pro
405 410 415

Lys Asp Glu Gln Val Pro Phe Ser Lys Glu Glu Cys Ala Phe Arg Ser
420 425 430

Gln Leu Glu Thr Pro Glu Thr Leu Leu Gly Ser Thr Glu Glu Lys Pro
435 440 445

Leu Pro Leu Gly Val Pro Asp Ala Gly Met Lys Pro Ser
450 455 460

<210> 33
<211> 1475
<212> DNA
<213> Homo sapiens

<400> 33
tccacctgtc cccgcagcgc cggctcgcgc cctcctgccg cagccaccga gccgccgtct 60

agcgccccga cctcgccacc atgagagccc tgctggcgcg cctgcttctc tgcgtcctgg 120

tcgtgagcga ctccaaaggc agcaatgaac ttcatcaagt tccatcgaac tgtgactgtc 180

taaatggagg aacatgtgtg tccaacaagt acttctccaa cattcactgg tgcaactgcc 240

caaagaaatt cggagggcag cactgtgaaa tagataagtc aaaaacctgc tatgagggga 300

atggtcactt ttaccgagga aaggccagca ctgacaccat gggccggccc tgcctgccct 360

ggaactctgc cactgtcctt cagcaaacgt accatgccca cagatctgat gctcttcagc 420

tgggcctggg gaaacataat tactgcagga acccagacaa ccggaggcga ccctggtgct 480

atgtgcaggt gggcctaaag ccgcttgtcc aagagtgcat ggtgcatgac tgcgcagatg 540

gaaaaaagcc ctcctctcct ccagaagaat taaaatttca gtgtggccaa aagactctga 600

ggccccgctt taagattatt gggggagaat tcaccaccat cgagaaccag ccctggtttg 660

cggccatcta caggaggcac cggggggct ctgtcaccta cgtgtgtgga ggcagcctca 720 tcagcccttg ctgggtgatc agcgccacac actgcttcat tgattaccca aagaaggagg 780

actacatcgt ctacctgggt cgctcaaggc ttaactccaa cacgcaaggg gagatgaagt 840

ttgaggtgga aaacctcatc ctacacaagg actacagcgc tgacacgctt gctcaccaca 900

acgacattgc cttgctgaag atccgttcca aggagggcag gtgtgcgcag ccatcccgga 960

ctatacagac catctgcctg ccctcgatgt ataacgatcc ccagtttggc acaagctgtg 1020

agatcactgg ctttggaaaa gagaattcta ccgactatct ctatccggag cagctgaaga 1080

tgactgttgt gaagctgatt tcccaccggg agtgtcagca gccccactac tacggctctg 1140

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gagactcagg gggacccctc gtctgttccc tccaaggccg catgactttg actggaattg 1260

tgagctgggg ccgtggatgt gccctgaagg acaagccagg cgtctacacg agagtctcac 1320

acttcttacc ctggatccgc agtcacacca aggaagagaa tggcctggcc ctctgagggt 1380

ccccagggag gaaacgggca ccacccgctt tcttgctggt tgtcattttt gcagtagagt 1440

catctccatc agctgtaaga agagactggg aagat 1475

<210> 34
<211> 431
<212> PRT
<213> Homo sapiens

<400> 34

Met Arg Ala Leu Leu Ala Arg Leu Leu Leu Cys Val Leu Val Val Ser
1 5 10 15

Asp Ser Lys Gly Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp
20 25 30

Cys Leu Asn Gly Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile
35 40 45

His Trp Cys Asn Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile
50 55 60

Asp Lys Ser Lys Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly
65 70 75 80

Lys Ala Ser Thr Asp Thr Met Gly Arg Pro Cys Leu Pro Trp Asn Ser
85 90 95

```
Ala Thr Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu
            100                 105                 110

Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg
        115                 120                 125

Arg Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln
    130                 135                 140

Glu Cys Met Val His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro
145                 150                 155                 160

Pro Glu Glu Leu Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg
                165                 170                 175

Phe Lys Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp
            180                 185                 190

Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val
        195                 200                 205

Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His
    210                 215                 220

Cys Phe Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly
225                 230                 235                 240

Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val
                245                 250                 255

Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala His
            260                 265                 270

His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys
        275                 280                 285

Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr
    290                 295                 300

Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys
305                 310                 315                 320
```

```
Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val
                325                 330                 335

Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly
            340                 345                 350

Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys
        355                 360                 365

Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu
    370                 375                 380

Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys
385                 390                 395                 400

Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu
                405                 410                 415

Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
            420                 425                 430


<210>  35
<211>  107
<212>  PRT
<213>  Mus musculus

<400>  35

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Val Asn Thr Ala
            20                  25                  30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Thr Thr Pro Pro
```

85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 36
<211> 120
<212> PRT
<213> Mus musculus

<400> 36

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Lys Asp Thr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 37
<211> 120
<212> PRT
<213> Mus musculus

<400> 37

Gln Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln
1 5 10 15

```
Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser
            20                  25                  30

Gly Met Ser Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Ala Leu Glu
        35                  40                  45

Trp Leu Ala Asp Ile Trp Trp Asp Asp Lys Lys Asp Tyr Asn Pro Ser
    50                  55                  60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val
65                  70                  75                  80

Val Leu Lys Val Thr Asn Met Asp Pro Ala Asp Thr Ala Thr Tyr Tyr
                85                  90                  95

Cys Ala Arg Ser Met Ile Thr Asn Trp Tyr Phe Asp Val Trp Gly Ala
            100                 105                 110

Gly Thr Thr Val Thr Val Ser Ser
        115                 120


<210>  38
<211>  106
<212>  PRT
<213>  Mus musculus

<400>  38

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Lys Cys Gln Leu Ser Val Gly Tyr Met
            20                  25                  30

His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Trp Ile Tyr
        35                  40                  45

Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
    50                  55                  60

Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp
65                  70                  75                  80

Asp Phe Ala Thr Tyr Tyr Cys Phe Gln Gly Ser Gly Tyr Pro Phe Thr
                85                  90                  95
```

```
Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100                 105


<210>  39
<211>  1039
<212>  DNA
<213>  Homo sapiens

<400>  39
tcctgcacag gcagtgcctt gaagtgcttc ttcagagacc tttcttcata gactactttt      60

ttttctttaa gcagcaaaag gagaaaattg tcatcaaagg atattccaga ttcttgacag     120

cattctcgtc atctctgagg acatcaccat catctcagga tgaggggcat gaagctgctg     180

ggggcgctgc tggcactggc ggccctactg caggggggccg tgtccctgaa gatcgcagcc     240

ttcaacatcc agacatttgg ggagaccaag atgtccaatg ccaccctcgt cagctacatt     300

gtgcagatcc tgagccgcta tgacatcgcc ctggtccagg aggtcagaga cagccacctg     360

actgccgtgg ggaagctgct ggacaacctc aatcaggatg caccagacac ctatcactac     420

gtggtcagtg agccactggg acggaacagc tataaggagc gctacctgtt cgtgtacagg     480

cctgaccagg tgtctgcggt ggacagctac tactacgatg atggctgcga gccctgcggg     540

aacgacacct tcaaccgaga gccagccatt gtcaggttct tctcccggtt cacagaggtc     600

agggagtttg ccattgttcc cctgcatgcg gccccggggg acgcagtagc cgagatcgac     660

gctctctatg acgtctacct ggatgtccaa gagaaatggg gcttggagga cgtcatgttg     720

atgggcgact tcaatgcggg ctgcagctat gtgagaccct cccagtggtc atccatccgc     780

ctgtggacaa gccccacctt ccagtggctg atccccgaca gcgctgacac cacagctaca     840

cccacgcact gtgcctatga caggatcgtg gttgcaggga tgctgctccg aggcgccgtt     900

gttcccgact cggctcttcc ctttaacttc caggctgcct atggcctgag tgaccaactg     960

gcccaagcca tcagtgacca ctatccagtg gaggtgatgc tgaagtgagc agcccctccc    1020

cacaccagtt gaactgcag                                                 1039


<210>  40
<211>  282
<212>  PRT
<213>  Homo sapiens

<400>  40

Met Arg Gly Met Lys Leu Leu Gly Ala Leu Leu Ala Leu Ala Ala Leu
```

```
1               5                   10                  15

Leu Gln Gly Ala Val Ser Leu Lys Ile Ala Ala Phe Asn Ile Gln Thr
            20                  25                  30

Phe Gly Glu Thr Lys Met Ser Asn Ala Thr Leu Val Ser Tyr Ile Val
        35                  40                  45

Gln Ile Leu Ser Arg Tyr Asp Ile Ala Leu Val Gln Glu Val Arg Asp
    50                  55                  60

Ser His Leu Thr Ala Val Gly Lys Leu Leu Asp Asn Leu Asn Gln Asp
65                  70                  75                  80

Ala Pro Asp Thr Tyr His Tyr Val Val Ser Glu Pro Leu Gly Arg Asn
                85                  90                  95

Ser Tyr Lys Glu Arg Tyr Leu Phe Val Tyr Arg Pro Asp Gln Val Ser
            100                 105                 110

Ala Val Asp Ser Tyr Tyr Tyr Asp Asp Gly Cys Glu Pro Cys Gly Asn
        115                 120                 125

Asp Thr Phe Asn Arg Glu Pro Ala Ile Val Arg Phe Phe Ser Arg Phe
    130                 135                 140

Thr Glu Val Arg Glu Phe Ala Ile Val Pro Leu His Ala Ala Pro Gly
145                 150                 155                 160

Asp Ala Val Ala Glu Ile Asp Ala Leu Tyr Asp Val Tyr Leu Asp Val
                165                 170                 175

Gln Glu Lys Trp Gly Leu Glu Asp Val Met Leu Met Gly Asp Phe Asn
            180                 185                 190

Ala Gly Cys Ser Tyr Val Arg Pro Ser Gln Trp Ser Ser Ile Arg Leu
        195                 200                 205

Trp Thr Ser Pro Thr Phe Gln Trp Leu Ile Pro Asp Ser Ala Asp Thr
    210                 215                 220

Thr Ala Thr Pro Thr His Cys Ala Tyr Asp Arg Ile Val Val Ala Gly
225                 230                 235                 240
```

Met Leu Leu Arg Gly Ala Val Val Pro Asp Ser Ala Leu Pro Phe Asn
245 250 255

Phe Gln Ala Ala Tyr Gly Leu Ser Asp Gln Leu Ala Gln Ala Ile Ser
260 265 270

Asp His Tyr Pro Val Glu Val Met Leu Lys
275 280

<210> 41
<211> 678
<212> DNA
<213> Mus musculus

<400> 41
gacatcttgc tgactcagtc tccagccatc ctgtctgtga gtccaggaga aagagtcagt 60

ttctcctgca gggccagtca gttcgttggc tcaagcatcc actggtatca gcaaagaaca 120

aatggttctc caaggcttct cataaagtat gcttctgagt ctatgtctgg gatcccttcc 180

aggtttagtg gcagtggatc agggacagat tttactctta gcatcaacac tgtggagtct 240

gaagatattg cagattatta ctgtcaacaa agtcatagct ggccattcac gttcggctcg 300

gggacaaatt tggaagtaaa agaagtgaag cttgaggagt ctggaggagg cttggtgcaa 360

cctggaggat ccatgaaact ctcctgtgtt gcctctggat tcattttcag taaccactgg 420

atgaactggg tccgccagtc tccagagaag gggcttgagt gggttgctga aattagatca 480

aaatctatta attctgcaac acattatgcg gagtctgtga aagggaggtt caccatctca 540

agagatgatt ccaaaagtgc tgtctacctg caaatgaccg acttaagaac tgaagacact 600

ggcgtttatt actgttccag gaattactac ggtagtacct acgactactg gggccaaggc 660

accactctca cagtctcc 678

<210> 42
<211> 226
<212> PRT
<213> Mus musculus

<400> 42

Asp Ile Leu Leu Thr Gln Ser Pro Ala Ile Leu Ser Val Ser Pro Gly
1 5 10 15

Glu Arg Val Ser Phe Ser Cys Arg Ala Ser Gln Phe Val Gly Ser Ser

20 25 30

Ile His Trp Tyr Gln Gln Arg Thr Asn Gly Ser Pro Arg Leu Leu Ile
35 40 45

Lys Tyr Ala Ser Glu Ser Met Ser Gly Ile Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Ser Ile Asn Thr Val Glu Ser
65 70 75 80

Glu Asp Ile Ala Asp Tyr Tyr Cys Gln Gln Ser His Ser Trp Pro Phe
85 90 95

Thr Phe Gly Ser Gly Thr Asn Leu Glu Val Lys Glu Val Lys Leu Glu
100 105 110

Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Met Lys Leu Ser
115 120 125

Cys Val Ala Ser Gly Phe Ile Phe Ser Asn His Trp Met Asn Trp Val
130 135 140

Arg Gln Ser Pro Glu Lys Gly Leu Glu Trp Val Ala Glu Ile Arg Ser
145 150 155 160

Lys Ser Ile Asn Ser Ala Thr His Tyr Ala Glu Ser Val Lys Gly Arg
165 170 175

Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ala Val Tyr Leu Gln Met
180 185 190

Thr Asp Leu Arg Thr Glu Asp Thr Gly Val Tyr Tyr Cys Ser Arg Asn
195 200 205

Tyr Tyr Gly Ser Thr Tyr Asp Tyr Trp Gly Gln Gly Thr Thr Leu Thr
210 215 220

Val Ser
225

<210> 43
<211> 450

```
<212>  DNA
<213>  Homo sapiens

<400>  43
gctgcatcag aagaggccat caagcacatc actgtccttc tgccatggcc ctgtggatgc      60

gcctcctgcc cctgctggcg ctgctggccc tctggggacc tgacccagcc gcagcctttg     120

tgaaccaaca cctgtgcggc tcacacctgg tggaagctct ctacctagtg tgcggggaac     180

gaggcttctt ctacacaccc aagacccgcc gggaggcaga ggacctgcag gtggggcagg     240

tggagctggg cgggggccct ggtgcaggca gcctgcagcc cttggccctg gaggggtccc     300

tgcagaagcg tggcattgtg gaacaatgct gtaccagcat ctgctccctc taccagctgg     360

agaactactg caactagacg cagcccgcag gcagcccccc acccgccgcc tcctgcaccg     420

agagagatgg aataaagccc ttgaaccagc                                      450


<210>  44
<211>  110
<212>  PRT
<213>  Homo sapiens

<400>  44

Met Ala Leu Trp Met Arg Leu Leu Pro Leu Leu Ala Leu Leu Ala Leu
1               5                   10                  15


Trp Gly Pro Asp Pro Ala Ala Ala Phe Val Asn Gln His Leu Cys Gly
            20                  25                  30


Ser His Leu Val Glu Ala Leu Tyr Leu Val Cys Gly Glu Arg Gly Phe
        35                  40                  45


Phe Tyr Thr Pro Lys Thr Arg Arg Glu Ala Glu Asp Leu Gln Val Gly
    50                  55                  60


Gln Val Glu Leu Gly Gly Gly Pro Gly Ala Gly Ser Leu Gln Pro Leu
65                  70                  75                  80


Ala Leu Glu Gly Ser Leu Gln Lys Arg Gly Ile Val Glu Gln Cys Cys
                85                  90                  95


Thr Ser Ile Cys Ser Leu Tyr Gln Leu Glu Asn Tyr Cys Asn
            100                 105                 110


<210>  45
```

<211> 1203
<212> DNA
<213> Hepatitis B virus

<400> 45
atgggaggtt ggtcttccaa acctcgacaa ggcatgggga cgaatctttc tgttcccaat 60

cctctgggat tctttcccga tcaccagttg gaccctgcgt tcggagccaa ctcaaacaat 120

ccagattggg acttcaaccc caacaaggat cactggccag aggcaatcaa ggtaggagcg 180

ggagacttcg ggccagggtt caccccacca cacggcggtc ttttggggtg gagccctcag 240

gctcagggca tattgacaac agtgccagca gcgcctcctc ctgtttccac caatcggcag 300

tcaggaagac agcctactcc catctctcca cctctaagag acagtcatcc tcaggccatg 360

cagtggaact ccacaacatt ccaccaagct ctgctagatc ccagagtgag gggcctatat 420

tttcctgctg gtggctccag ttccggaaca gtaaaccctg ttccgactac tgtctcaccc 480

atatcgtcaa tcttctcgag gactggggac cctgcaccga acatggagag cacaacatca 540

ggattcctag gacccctgct cgtgttacag gcggggtttt tcttgttgac aagaatcctc 600

acaataccac agagtctaga ctcgtggtgg acttctctca attttctagg gggagcaccc 660

acgtgtcctg gccaaaattc gcagtcccca acctccaatc actcaccaac ctcttgtcct 720

ccaatttgtc ctggttatcg ctggatgtgt ctgcggcgtt ttatcatatt cctcttcatc 780

ctgctgctat gcctcatctt cttgttggtt cttctggact accaaggtat gttgcccgtt 840

tgtcctctac ttccaggaac atcaactacc agcacgggac catgcaagac ctgcacgatt 900

cctgctcaag gaacctctat gtttccctct tgttgctgta caaaaccttc ggacggaaac 960

tgcacttgta ttcccatccc atcatcctgg gctttcgcaa gattcctatg ggagtgggcc 1020

tcagtccgtt tctcctggct cagtttacta gtgccatttg ttcagtggtt cgcagggctt 1080

tcccccactg tttggctttc agttatatgg atgatgtggt attgggggcc aagtctgtac 1140

aacatcttga gtcccttttt acctctatta ccaattttct tttgtctttg ggtatacatt 1200

tga 1203

<210> 46
<211> 400
<212> PRT
<213> Hepatitis B virus

<400> 46

Met Gly Gly Trp Ser Ser Lys Pro Arg Gln Gly Met Gly Thr Asn Leu
1 5 10 15

```
Ser Val Pro Asn Pro Leu Gly Phe Phe Pro Asp His Gln Leu Asp Pro
            20                  25                  30

Ala Phe Gly Ala Asn Ser Asn Asn Pro Asp Trp Asp Phe Asn Pro Asn
        35                  40                  45

Lys Asp His Trp Pro Glu Ala Ile Lys Val Gly Ala Gly Asp Phe Gly
    50                  55                  60

Pro Gly Phe Thr Pro Pro His Gly Gly Leu Leu Gly Trp Ser Pro Gln
65                  70                  75                  80

Ala Gln Gly Ile Leu Thr Thr Val Pro Ala Ala Pro Pro Pro Val Ser
                85                  90                  95

Thr Asn Arg Gln Ser Gly Arg Gln Pro Thr Pro Ile Ser Pro Pro Leu
            100                 105                 110

Arg Asp Ser His Pro Gln Ala Met Gln Trp Asn Ser Thr Thr Phe His
        115                 120                 125

Gln Ala Leu Leu Asp Pro Arg Val Arg Gly Leu Tyr Phe Pro Ala Gly
    130                 135                 140

Gly Ser Ser Ser Gly Thr Val Asn Pro Val Pro Thr Thr Val Ser Pro
145                 150                 155                 160

Ile Ser Ser Ile Phe Ser Arg Thr Gly Asp Pro Ala Pro Asn Met Glu
                165                 170                 175

Ser Thr Thr Ser Gly Phe Leu Gly Pro Leu Leu Val Leu Gln Ala Gly
            180                 185                 190

Phe Phe Leu Leu Thr Arg Ile Leu Thr Ile Pro Gln Ser Leu Asp Ser
        195                 200                 205

Trp Trp Thr Ser Leu Asn Phe Leu Gly Gly Ala Pro Thr Cys Pro Gly
    210                 215                 220

Gln Asn Ser Gln Ser Pro Thr Ser Asn His Ser Pro Thr Ser Cys Pro
225                 230                 235                 240
```

```
Pro Ile Cys Pro Gly Tyr Arg Trp Met Cys Leu Arg Arg Phe Ile Ile
                245                 250                 255

Phe Leu Phe Ile Leu Leu Leu Cys Leu Ile Phe Leu Leu Val Leu Leu
            260                 265                 270

Asp Tyr Gln Gly Met Leu Pro Val Cys Pro Leu Leu Pro Gly Thr Ser
        275                 280                 285

Thr Thr Ser Thr Gly Pro Cys Lys Thr Cys Thr Ile Pro Ala Gln Gly
    290                 295                 300

Thr Ser Met Phe Pro Ser Cys Cys Cys Thr Lys Pro Ser Asp Gly Asn
305                 310                 315                 320

Cys Thr Cys Ile Pro Ile Pro Ser Ser Trp Ala Phe Ala Arg Phe Leu
                325                 330                 335

Trp Glu Trp Ala Ser Val Arg Phe Ser Trp Leu Ser Leu Leu Val Pro
            340                 345                 350

Phe Val Gln Trp Phe Ala Gly Leu Ser Pro Thr Val Trp Leu Ser Val
        355                 360                 365

Ile Trp Met Met Trp Tyr Trp Gly Pro Ser Leu Tyr Asn Ile Leu Ser
    370                 375                 380

Pro Phe Leu Pro Leu Leu Pro Ile Phe Phe Cys Leu Trp Val Tyr Ile
385                 390                 395                 400


<210>  47
<211>  799
<212>  DNA
<213>  Homo sapiens

<400>  47
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cccaaccatt cccttatcca ggccttttga caacgctatg ctccgcgccc atcgtctgca     180

ccagctggcc tttgacacct accaggagtt tgaagaagcc tatatcccaa aggaacagaa     240

gtattcattc ctgcagaacc cccagacctc cctctgtttc tcagagtcta ttccgacacc     300
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ctccaacagg gaggaaacac aacagaaatc caacctagag ctgctccgca tctccctgct     360

gctcatccag tcgtggctgg agcccgtgca gttcctcagg agtgtcttcg ccaacagcct     420

ggtgtacggc gcctctgaca gcaacgtcta tgacctccta aaggacctag aggaaggcat     480

ccaaacgctg atggggaggc tggaagatgg cagcccccgg actgggcaga tcttcaagca     540

gacctacagc aagttcgaca caaactcaca caacgatgac gcactactca agaactacgg     600

gctgctctac tgcttcagga aggacatgga caaggtcgag acattcctgc gcatcgtgca     660

gtgccgctct gtggagggca gctgtggctt ctagctgccc gggtggcatc cctgtgaccc     720

ctccccagtg cctctcctgg ccctggaagt tgccactcca gtgcccacca gccttgtcct     780

aataaaatta agttgcatc                                                  799
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<210>  48
<211>  217
<212>  PRT
<213>  Homo sapiens

<400>  48

Met Ala Thr Gly Ser Arg Thr Ser Leu Leu Leu Ala Phe Gly Leu Leu
1               5                   10                  15

Cys Leu Pro Trp Leu Gln Glu Gly Ser Ala Phe Pro Thr Ile Pro Leu
            20                  25                  30

Ser Arg Pro Phe Asp Asn Ala Met Leu Arg Ala His Arg Leu His Gln
        35                  40                  45

Leu Ala Phe Asp Thr Tyr Gln Glu Phe Glu Glu Ala Tyr Ile Pro Lys
    50                  55                  60

Glu Gln Lys Tyr Ser Phe Leu Gln Asn Pro Gln Thr Ser Leu Cys Phe
65                  70                  75                  80

Ser Glu Ser Ile Pro Thr Pro Ser Asn Arg Glu Glu Thr Gln Gln Lys
                85                  90                  95

Ser Asn Leu Glu Leu Leu Arg Ile Ser Leu Leu Leu Ile Gln Ser Trp
            100                 105                 110

Leu Glu Pro Val Gln Phe Leu Arg Ser Val Phe Ala Asn Ser Leu Val
        115                 120                 125
```

Tyr Gly Ala Ser Asp Ser Asn Val Tyr Asp Leu Leu Lys Asp Leu Glu
    130   135   140

Glu Gly Ile Gln Thr Leu Met Gly Arg Leu Glu Asp Gly Ser Pro Arg
145   150   155   160

Thr Gly Gln Ile Phe Lys Gln Thr Tyr Ser Lys Phe Asp Thr Asn Ser
                165   170   175

His Asn Asp Asp Ala Leu Leu Lys Asn Tyr Gly Leu Leu Tyr Cys Phe
            180   185   190

Arg Lys Asp Met Asp Lys Val Glu Thr Phe Leu Arg Ile Val Gln Cys
        195   200   205

Arg Ser Val Glu Gly Ser Cys Gly Phe
    210   215

<210> 49
<211> 963
<212> DNA
<213> Homo sapiens

<400> 49
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acgccgcggc cgaaaccggc cggggccagc agccctgcgc ccaggacggc gctgcagccg 240

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cacgaagacc ctgaggtcaa gttcaactgg tacgtggacg gcgtggaggt gcataatgcc 480

aagacaaagc cgcgggagga gcagtacaac agcacgtacc gtgtggtcag cgtcctcacc 540

gtcctgcacc aggactggct gaatggcaag gagtacaagt gcaaggtctc caacaaagcc 600

ctcccagccc ccatcgagaa aaccatctcc aaagccaaag ggcagccccg agaaccacag 660

gtgtacaccc tgcccccatc ccgggatgag ctgaccaaga accaggtcag cctgacctgc 720

ctggtcaaag gcttctatcc cagcgacatc gccgtggagt gggagagcaa tgggcagccg 780 gagaacaact acaagaccac gcctcccgtg ttggactccg acggctcctt cttcctctac 840

agcaagctca ccgtggacaa gagcaggtgg cagcagggga acgtcttctc atgctccgtg 900

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tga 963

<210> 50
<211> 320
<212> PRT
<213> Homo sapiens

<400> 50

Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
1 5 10 15

Gly Ser Thr Gly Asp Val Arg Arg Gly Pro Arg Ser Leu Arg Gly Arg
20 25 30

Asp Ala Pro Ala Pro Thr Pro Cys Val Pro Ala Glu Cys Phe Asp Leu
35 40 45

Leu Val Arg His Cys Val Ala Cys Gly Leu Leu Arg Thr Pro Arg Pro
50 55 60

Lys Pro Ala Gly Ala Ser Ser Pro Ala Pro Arg Thr Ala Leu Gln Pro
65 70 75 80

Gln Glu Ser Val Gly Ala Gly Ala Gly Glu Ala Ala Val Asp Lys Thr
85 90 95

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
100 105 110

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
115 120 125

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
130 135 140

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
145 150 155 160

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val

165 170 175

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
180 185 190

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
195 200 205

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
210 215 220

Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys
225 230 235 240

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
245 250 255

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
260 265 270

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
275 280 285

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
290 295 300

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
305 310 315 320

<210> 51
<211> 107
<212> PRT
<213> Homo sapiens

<400> 51

Asp Ile Gln Met Thr Gln Thr Pro Ser Thr Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Asn Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Asp Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Val Lys
            100   105

<210> 52
<211> 107
<212> PRT
<213> Mus musculus

<400> 52

Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1   5   10   15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Asn Asn Tyr
            20   25   30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Ile Val Lys Leu Leu Ile
        35   40   45

Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65   70   75   80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp
                85   90   95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100   105

<210> 53
<211> 119
<212> PRT
<213> Homo sapiens

<400> 53

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr
20 25 30

Leu Ile Glu Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Val Asp Glu Ser Thr Asn Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 54
<211> 119
<212> PRT
<213> Mus musculus

<400> 54

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Gly Pro Gly Thr
1 5 10 15

Ser Val Arg Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr
20 25 30

Leu Ile Glu Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Thr Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Asp Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Arg Gly
100 105 110

Thr Leu Val Thr Val Ser Ala
115

<210> 55
<211> 214
<212> PRT
<213> Homo sapiens

<400> 55

Asp Ile Gln Met Thr Gln Thr Pro Ser Thr Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Asn Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Val Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 56
<211> 448
<212> PRT
<213> Homo sapiens

<400> 56

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr
20 25 30

Leu Ile Glu Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Leu Thr Val Asp Glu Ser Thr Asn Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Gln Gly
100 105 110

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Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
        115                 120                 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
    130                 135                 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145                 150                 155                 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
                165                 170                 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
            180                 185                 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
        195                 200                 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
    210                 215                 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225                 230                 235                 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
                245                 250                 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
            260                 265                 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
        275                 280                 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
    290                 295                 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305                 310                 315                 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
                325                 330                 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
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            340                 345                 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
        355                 360                 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
    370                 375                 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385                 390                 395                 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
                405                 410                 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
            420                 425                 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
        435                 440                 445


<210>  57
<211>  8540
<212>  DNA
<213>  Homo sapiens

<400>  57
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aggccgaggc ggcctcggcc tctgcataaa taaaaaaaat tagtcagcca tgcatggggc     120

ggagaatggg cggaactggg cggagttagg ggcgggatgg gcggagttag gggcgggact     180

atggttgctg actaattgag atgcatgctt tgcatacttc tgcctgctgg ggagcctggg     240

gactttccac acctggttgc tgactaattg agatgcatgc tttgcatact tctgcctgct     300

ggggagcctg gggactttcc acaccctaac tgacacacat tccacagaat taattcccct     360

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gttacataac ttacggtaaa tggcccgcct ggctgaccgc ccaacgaccc ccgcccattg     480

acgtcaataa tgacgtatgt tcccatagta acgccaatag ggactttcca ttgacgtcaa     540

tgggtggact atttacggta aactgcccac ttggcagtac atcaagtgta tcatatgcca     600

agtacgcccc ctattgacgt caatgacggt aaatggcccg cctggcatta tgcccagtac     660

atgaccttat gggactttcc tacttggcag tacatctacg tattagtcat cgctattacc     720
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cggtgggagg tctatataag cagagctggg tacgtgaacc gtcagatcgc ctggagacgc 960

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cgtagagcca caccttggta agggccaatc tgctcacaca ggatagagag ggcaggagcc 5160

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Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val
            100                 105                 110

Tyr Tyr Cys Ala Arg Ser Thr Tyr Tyr Gly Gly Asp Trp Tyr Phe Asn
        115                 120                 125

Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ala
    130                 135                 140
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